Problem Based Urology

Paolo Gontero
Roger S. Kirby
Culley C. Carson III
Editors



Springer

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In memory of Silvia, my beloved sister.

Paolo

Foreword

As the authors of this book state in their Preface, their aim is to produce something which is user-friendly and is primarily intended for general practitioners. The authors also mention that urological problems represent a significant amount of work for primary care physicians in their everyday practice. Their purpose, therefore, was to address the concerns which general practitioners might have relating to diagnosis and treatment of urological conditions and when to refer them for specialist care.

This excellent book fully addresses these problems and will make the task of deciding which patients need to be referred on for specialist evaluation a great deal easier. In order to facilitate this the urological problems are presented here in a rather novel way, in that there are three sections which cover different ways in which these conditions may present: either as urological symptoms, or urological abnormalities on imaging or as urological abnormalities on blood and urine testing. The decision charts and the explanatory text in this book should ensure that those individuals who need further investigation are appropriately cared for, while those whom it is safe to treat in primary care are not needlessly sent into the hospital system. Against a background of stretched healthcare budgets and increasing litigation against doctors, for among other things, delayed and misdiagnosis, this volume could hardly have been more timely.

I would like to congratulate the authors on editing a highly informative and educational volume, which addresses an important issue and is also easy to read.

John M. Fitzpatrick
MCh, FRCSI, FEBU, FC Urol (SA), FRCSGlas, FRCS

Preface

Dear reader,
This book is primarily intended for general practitioners as an aid to in dealing with urological problems, which currently represent a significant burden in their everyday practice.

One of the major concerns for GPs is how far to go themselves in the diagnosis and treatment of the most commonly encountered urological diseases or when to refer the patient for specialist care. As specialists in the field of urology, we have attempted to provide a user-friendly guide to decision making in the major urological problems. We have made suggestions for the most appropriate timing for referral to specialist care and the types of information (investigations) with which the patients should be referred to the specialist.

Urological problems have been grouped into three sections, addressing urological symptoms (Part I), urological abnormalities on imaging (Part II), and urological abnormalities on blood and urine tests (Part III). The chapters have been covered by internationally recognized experts in each specific field. Flow charts and tables are intended to guide the reader, step by step, through the differential diagnosis for each urological problem.

We have tried to emphasize the key position of GPs in leading the diagnosis and treatment of most urological problems, resulting in a more appropriate specialist referral.

We hope we have succeeded in our task!

Paolo Gontero
Roger S. Kirby
Culley C. Carson III

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The editors wish to express immense gratitude to their coauthors, all internationally recognized experts in the fields of urology and nephrology, for their commitment and outstanding contributions to this book.

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Part I
Decision Making Based on Patients' Reported Symptoms

Chapter 1
Flank Pain/Renal Colic

Paolo Gontero and Alessandro Tizzani

Abstract A number of different medical conditions can cause a pain in the loin and/or in the flank. Several urological diseases affecting the upper urinary tract need to be considered in the differential diagnosis. Among these, renal colic (defined as a severe visceral pain of sudden onset due to abrupt distension of the urinary collecting system and/or stretching of the renal capsule) plays a major role since its main cause, a urinary stone, is a highly probable event among both sexes. The aim of this chapter is to guide the GP through the sometimes "tricky" differential diagnosis of loin/flank pain, starting from a careful consideration of the type of pain, moving on to a brief description of the main possible clinical situations, and finally presenting some decision-making algorithms. Any patient with acute flank pain/renal colic should be investigated, bearing in mind that while a renal stone is the most likely underlying condition, other renal (kidney infection) or extrarenal diseases (aortic aneurysm) need to be ruled out. An acute flank pain/renal colic associated with one or more of the following conditions (elderly patient or vascular comorbidities, fever, pregnancy, anuria, pain in the side of a solitary kidney, and pain persistence after IM or IV administration of NSAIDs or opioids) needs an urgent hospital referral. Asymptomatic patients with a history of flank pain/renal colic, in the absence of the above complications, are amenable to deferred management.

Keywords Renal colic • Flank pain • Differential diagnosis • Urinary calculi • Complicated • Kidney infection • Aortic aneurysm • Treatment

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Introduction

A number of different medical conditions can cause a pain in the loin and/or in the flank. Most of these lack specific accompanying features which means that making an accurate diagnosis is sometimes difficult. Several urological diseases affecting the upper urinary tract need to be considered in the differential diagnosis. Among these, renal colic (defined as a severe visceral pain of sudden onset due to abrupt distension of the urinary collecting system and/or stretching of the renal capsule) plays a major role since its main cause, a urinary stone, is a highly probable event among both sexes.

The aim of this chapter is to guide the GP through the sometimes "tricky" differential diagnosis of loin/flank pain, starting from a careful consideration of the type of pain, moving on to a brief description of the main possible clinical situations, and finally presenting some decision-making algorithms.

What Kind of Pain Is It? Is It Just a "Flank Pain" or Renal Colic?

In the sometimes difficult attempt to identify the correct cause of a flank pain, it may be helpful to try to discern whether the pain is of visceral origin (i.e., due to the distension of an organ like the kidney) or of somatic origin (i.e., as a consequence of irritation of the peritoneum). Table 1.1 reports the comparative characteristics of both types of pain to guide to a correct diagnosis.

One of the most common presentations of a flank pain of renal origin is renal colic. *Renal colic* is an acute flank pain, a typical visceral pain, provoked by the abrupt distension of the renal capsule or the urinary collecting system. The most common reason for the pain is a sudden blockage of the urine drainage at any level of the upper urinary tract due to a stone. It typically presents with a loin/flank pain of severe intensity, starting with a sudden onset and evolving in an intermittent way. It may radiate either anteriorly toward the hypochondrium (thus, sometimes difficult

Table 1.1 Comparative characteristics of the two main types of pain: visceral and somatic

Type of pain	Origin	Etiology	Pain characteristics	Patient appearance
Visceral	Any parenchymal (kidney) or cavitated organ (bowel, gallbladder)	Distension or contraction of an organ	Intermittent, crampy, difficult to localize	Constantly moving as he/she cannot find the right position
Somatic	Abdominal wall, peritoneal and retroperitoneal cavities	Peritoneal irritation	Continuous, stabbing, more localized	Immobile (any body movement increases the pain)

to differentiate from an abdominal visceral pain) or antero-inferiorly to the iliac fossa (sometimes mimicking a somatic abdominal pain such as that due to a peritoneal irritation) or, more commonly, to the male groin or testicle and the female vulva or labia. Not unusually, nausea and vomiting worsen the clinical course of renal colic. When a stone is located at the ureterovesical junction, dysuria and frequency become common accompanying symptoms.

When not caused by renal colic, flank pain is characterized by a dull, continuous pain, of milder intensity compared to renal colic and usually with no other accompanying symptoms. It can be described either as a sensation of "heaviness" or as a constant "itching". While a renal origin (due, e.g., to an obstruction in the urinary tract of gradual onset) is one likely explanation, a number of different diseases (including a somatic pain of vertebral origin due to, e.g., a radiculitis) can challenge a correct diagnosis.

What Is Causing Flank Pain or Renal Colic? Make a Differential Diagnosis

Renal colic does not always equate to stones in the same way that flank pain does not always equate to kidney disease.

It has always to be kept in mind that:

1. Several upper urinary tract diseases other than a stone may result in renal colic or flank pain.
2. A number of extrarenal diseases, some of them serious, may mimic renal colic and need therefore to be promptly identified.

Table 1.2 reports the main clinical conditions affecting the upper urinary tract/kidney, while Table 1.3 lists the most common diseases arising outside the upper urinary tract that may present with flank pain or with symptoms mimicking renal colic. Some hints related to the patient's history, symptoms or signs, and urine dipstick findings (easily feasible in the GP's office) are provided for each disease to aid in the initial differential diagnosis.

GP Management of Flank Pain/Renal Colic

Essentially, two main clinical scenarios may face the GP when assessing a patient with flank pain/renal colic:

- The patient seeking help is in agony because of an acute flank pain, potentially suggestive of renal colic. This clinical situation will be addressed in Flowchart 1.1.
- Another common situation pertains to the asymptomatic patient who comes to the GP with a history of acute flank pain/renal colic. Flowchart 1.2 will address how to manage this clinical scenario.

Table 1.2 Main diseases of the upper urinary tract that most often present with renal colic (although sometimes they may only cause flank pain)

Disease	Patient's history	Symptoms and signs
Urinary stone	Previous history of urinary stone	Pain significantly worsened during bimanual kidney examination,[a] microscopic hematuria on urine dipstick
Obstruction of the ureteropelvic junction	Known abnormalities of the upper urinary tract, pain may follow the ingestion of large amounts of fluid	Pain significantly worsened during bimanual kidney examination, urine dipstick is usually normal
Pyelonephritis	Female sex, recurrent urinary tract infections, vesicoureteral reflux	Flank pain relatively milder than that of renal colic; fever and chills very common. Suprapubic pain with dysuria, frequency, and urgency often accompanying. Pyuria typically detected on urine dipstick
Renal abscesses	Diabetics at increased risk; suspect renal abscess in any patient with pyelonephritis who does not improve with antibiotic therapy	Fever and chills are common. A palpable mass can be present. Sometimes decreased breath sounds on the affected side due to diaphragmatic irritation. Pyuria typically detected on urine dipstick
Papillary necrosis[b]	Female sex, diabetes, analgesic abuse	Pain significantly worsened during bimanual kidney examination, fever and chills, microscopic hematuria on urine dipstick
Blood clots	Recent diagnostic or surgical maneuvers on the kidney (renal biopsy, partial nephrectomy)	Hematuria
Acute renal infarction	Aged over 50, prior history of a thromboembolic event, chronic atrial fibrillation	Unilateral acute flank pain mimicking renal colic, hematuria and proteinuria on dipstick

[a]Bimanual kidney palpation allows examination of the kidney by lifting soft tissues below the costovertebral angle with one hand placed posteriorly while the anterior hand presses the abdomen firmly. It can be useful to determine the presence of a kidney mass (the normal kidney is usually not palpable) and to discriminate a tenderness arising from the kidney

[b]Papillary necrosis can cause an acute ureteral obstruction from a sloughed papilla caused by vascular ischemia, which leads to coagulative necrosis of the renal medullary pyramids

Comments About Flowchart 1.1

1. The most important clinical decision to take when approaching a patient with acute flank pain suggestive of renal colic is whether it is a complicated clinical condition or not. A brief medical history and examination of the patient will allow GPs to distinguish those with complications, needing to be urgently referred to A&E, from those for whom a conservative approach is worth trying.

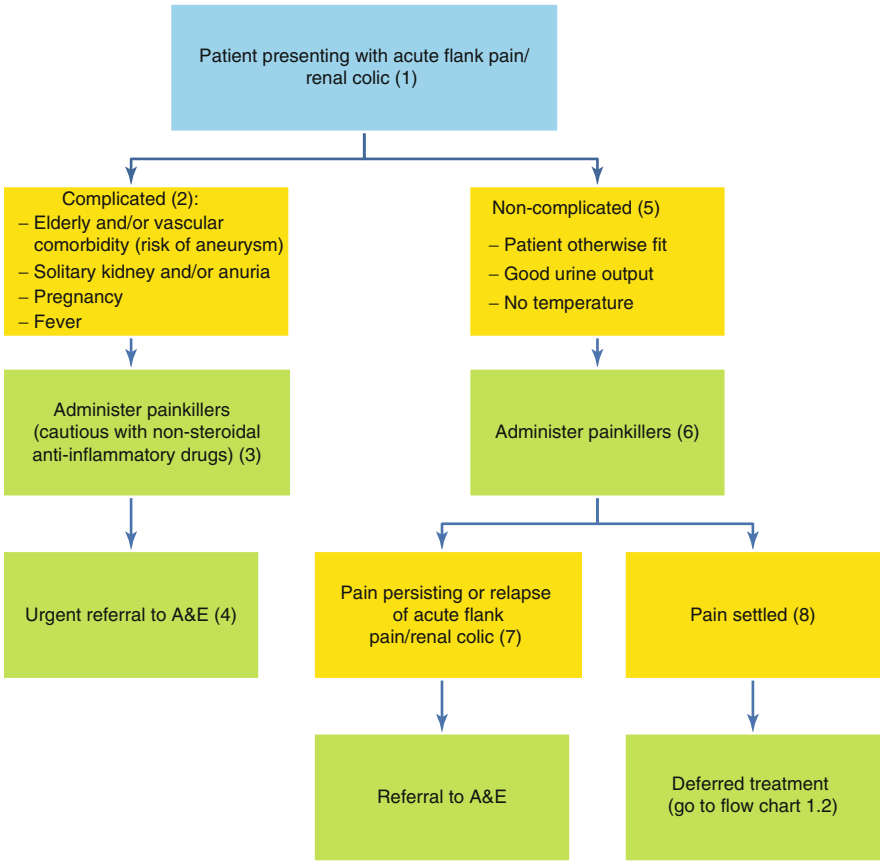
Table 1.3 Most common extrarenal diseases that can present with flank pain and sometimes may even mimic renal colic

Disease	Patient's history	Discriminating symptoms and signs
Abdominal aortic aneurysms[a]	Risk factors for atherosclerosis, aged patients	Abnormal mesogastric pulsation
Muscular pain	History of heavy lifting or repetitive bending at work	Dull aching discomfort in the thoracolumbar area. The affected area is usually tender when palpated
Radiculitis (injury of the lumbar or lower thoracic nerve roots)	Most patients are female. Predisposing factors include a history of rib fractures, arthritis, and a prior open renal surgery.	When the pain affects the 10th, 11th, or 12th ribs, the discomfort mimics renal colic in its distribution but is usually described as sharp or stabbing. Movement exacerbates the pain
Pleuritis and pneumonia	Respiratory symptoms or atypical pain involving the chest	Sharp stabbing pain in the thoracolumbar region which can simulate renal colic
Biliary colic	Known history of gallbladder stones	Pain location in the left hypochondrium with interscapular radiation; Murphy's sign
Acute appendicitis	–	Signs of peritonism (always absent in case of renal colic). Patient lies immobile in supine position to avoid worsening of the pain
Extrauterine pregnancy[b]	Young women, late or missed period	Positive pregnancy test, vaginal bleeding
Acute pancreatitis	Alcohol abuse	Epigastric pain
Herpes zoster	–	The pain is typically a burning pain (moderate to severe), localized in a very limited and demarcated band around the flank corresponding to a dermatome. Usually the pain precedes the appearance of typical vesicles

[a]In up to 10 % of cases, abdominal aortic aneurysms are misdiagnosed as renal colic
[b]An extrauterine pregnancy occurs when a fertilized egg implants outside the womb. It usually occurs in the fallopian tube but in rare cases can involve the ovary. The pain, usually located on the left iliac fossa, can sometimes radiate in the flank thus mimicking renal colic

2. Symptoms suggestive of renal colic are to be considered "complicated" when associated with at least one of the following clinical conditions:

 - Advanced age or vascular comorbidity, since the risk of a ruptured aneurysm is significant.
 - Fever, as it is highly suggestive of a kidney infection (pyelonephritis or infected stone), a clinical condition that carries a significant risk of urinary sepsis.
 - Acute flank pain/renal colic on the side of a solitary kidney: a stone in the only upper urinary tract may cause complete blockage of the urinary output leading

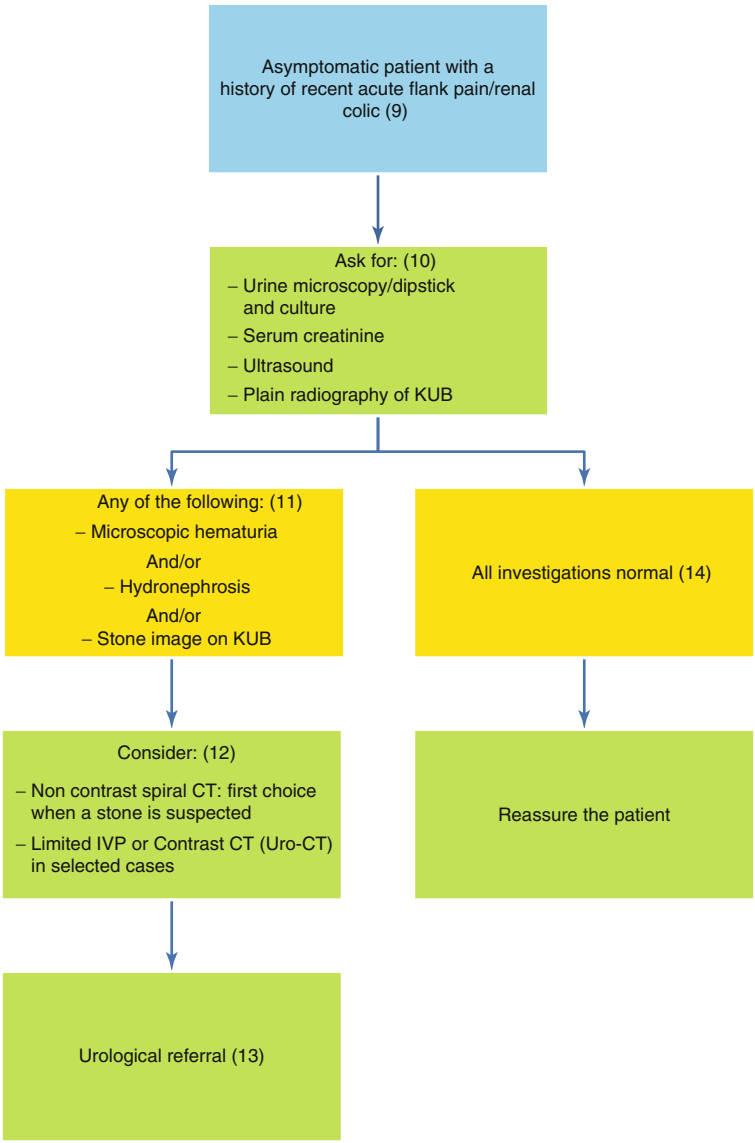


Flowchart 1.1 Patient presenting with acute flank pain/renal colic

to oliguria or anuria; scanty or no urine output in the presence of both kidneys may suggest the rare occurrence of bilateral ureteral stones.

- Pregnancy: a flank pain in a pregnant woman may be due to ureteral compression from the fetus, although the possibility of a kidney infection or urinary stone must always be kept in mind.

3. The first action to be taken in a patient with complicated renal colic is to ease the pain by administering a painkiller. Two main classes of drugs are used to relieve flank pain/renal colic that is usually of moderate to severe intensity: nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids. The most commonly used drugs and dosages are reported in Table 1.4. Administration of NSAIDs should be done with great care in patients with known or presumed reduction of renal function as they can further deteriorate renal function by causing constriction of the renal artery. In these cases, opioids represent a safer treatment option. During pregnancy, paracetamol can be administered safely, while opioids represent the second-line option in case of pain persistence, since



Flowchart 1.2 Asymptomatic patient with a history of recent acute flank pain/renal colic

NSAIDs are contraindicated. There is no proof of efficacy for antispastic therapies in the treatment of renal colic.

4. After administering the most appropriate pain relief, patients with complicated renal colic need an urgent referral to A&E.
5. A patient presenting in agony for symptoms suggestive of renal colic but otherwise in good clinical condition (no significant vascular comorbidities), no fever and claiming a normal urine output, is likely to suffer from a "noncomplicated" renal colic.

Table 1.4 Pain killers that can be used in cases of acute flank pain/renal colic

Type of pain killer	Molecule	Route of administration and dosage
Nonsteroidal anti-inflammatory drugs	Ketorolac	IV or IM, 30–60 mg, can be repeated every 6 h at a dose of 15 mg
		Oral, 10 mg every 4–6 h
	Diclofenac	IM, 75 mg
		Oral, 50 mg up to two to three times per day
Opioids	Meperidine	IM, 1 mg/Kg, can be repeated every 4 h
	Morphine sulfate	IV or IM, 0.1 mg/Kg, can be repeated every 4 h

IV intravenous, *IM* intramuscular

6. IM or IV administration of either a NSAID or an opioid (see Table 1.4) represents the first treatment option. In the absence of specific contraindications, NSAID may represent the first-line choice, while opioids can be used as second-line therapy in case of pain persistence. In the acute phase of the pain, high fluid intake is not recommended because it may worsen the pain when a ureteral stone is the underlying cause. In addition, there is no proof that high fluid intake is beneficial in stone expulsion.
7. Patients with persisting severe pain despite the administration of NSAID and/or opioids should be referred to A&E.
8. If the pain settles and does not recur following administration of painkillers, the patient can be safely managed according to Flowchart 1.2.

Comments About Flowchart 1.2

9. Any patient with a history of acute flank pain or symptoms suggestive of renal colic should be investigated further. The proposed algorithm aims to guide the GP through a minimum diagnostic work-up in order to optimize specialist referral.
10. It is advisable that all such patients undergo the following investigations:

 (a) In-office urine dipstick or urine sediment investigation from the laboratory.
 (b) Ultrasound (US): if history is highly suggestive of renal colic, the ultrasound may be limited to the urinary tract (kidney and bladder); a complete abdominal US is preferable when other causes of acute flank pain need to be excluded (biliary colic, aortic aneurysm, pancreatitis, etc.). US has a 90 % sensitivity for the detection of urinary tract obstruction but may miss ureteric stones that are not causing hydronephrosis.
 (c) A plain radiography of kidney, ureter, and bladder (KUB) should be another first-line investigation since it is cost effective with limited X-ray exposure for the patient. When performed alone, it has a sensitivity of no more than 50 % in identifying ureteric calculi. It typically identifies radiopaque stones but misses the radiolucent ones (such as acid uric stones). However, when combining US and plain radiography KUB, up to 80 % of urinary stones can be detected.

11. One or more of the following abnormal findings in the above investigations warrant further investigations: microscopic hematuria in the urine sediment examination; hydronephrosis on US (with or without the evidence of calculi); the suspicion of a urinary stone during the plain radiography KUB. Alternatively, the GP may decide to refer the patient to the urologist straightaway.
12. Nowadays the most accurate way of detecting calculi in the renal tract is non-contrast spiral computed tomography (CT). This has even been shown to be superior to intravenous pyelography (IVP), previously regarded as the gold standard investigation for urinary tract obstruction. Non-contrast CT allows a significant radiation dose reduction, which is important as renal colic patients are typically young and have a high rate of recurrent presentation. Non-contrast CT has a 97 % sensitivity for detecting calculi in the urinary tract. When non-contrast CT is unavailable, limited IVP or contrast CT are reasonable alternatives.
13. No matter what the results of spiral non-contrast CT or contrast investigations may be, patients with a history of acute flank pain/renal colic and the findings of either microscopic hematuria or hydronephrosis or urinary calculi require a urological referral.
14. When urine dipstick, US, and plain KUB all come back normal, a urological referral is not mandatory and the patient can be reassured.

Conclusions

Any patient with acute flank pain/renal colic should be investigated bearing in mind that while a renal stone is the most likely underlying condition, other renal (kidney infection) or extrarenal diseases (aortic aneurysm) need to be ruled out. Several factors will guide the GP's choice between an urgent hospital referral and an initial conservative management, including signs or symptoms of complicated renal colic and response to painkiller administration.

An acute flank pain/renal colic associated with one or more of the following conditions (elderly patient or vascular comorbidities, fever, pregnancy, anuria, pain in the side of a solitary kidney, pain persistence after IM or IV administration of NSAIDs or opioids) needs an urgent hospital referral. Asymptomatic patients with a history of flank pain/renal colic, in the absence of the above complications, are amenable to deferred management. A minimum diagnostic work-up with a urine dipstick, an abdominal ultrasound, and a plain radiography of KUB is advisable, leading to specialist referral in case of abnormal findings.

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Chapter 2
Lower Abdominal Pain/Suprapubic Pain

Paolo Gontero and Bruno Frea

Abstract The term "lower abdomen" refers to the portion of abdomen below the umbilicus in which three topographic regions can be identified: the hypogastrium in the middle and the left and right iliac fossa, both located lateral to the hypogastrium, in the left and right inferior part of the surface of the human abdomen, respectively. The majority of men and women will complain, at least once in their life, of a pain localized in the lower abdomen. For this reason, the number of GP's referrals because of a lower abdominal pain is expected to be high. A number of different diseases can cause a pain, of variable mode of presentation, intensity, and duration, in the left iliac fossa, the right iliac fossa, and the hypogastrium (this latter also termed suprapubic pain), respectively. These may arise from different organs (bowel, lower urinary tract, and female reproductive system) and thus potentially involve different specialists (general surgeon, urologist, and gynecologist). Importantly, the physician needs to suspect those few cases that need an urgent referral, i.e., extrauterine pregnancy in fertile females and cecal or sigmoid perforation, more common in elderly patients. The aim of this chapter is to provide general criteria (essentially based on patient's history and examination) that may lead a GP to suspect a urological origin of lower abdominal pain (and the need for a urological referral). The main features for the differential diagnosis with diseases belonging to other apparatus will also be provided in order to identify the most appropriate specialist referral.

Keywords Hypogastric pain • Suprapubic pain • Iliac fossa pain • Urine retention • Prostatitis • Appendicitis • Sigmoid diverticulosis • Adnexitis

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Introduction

The term "lower abdomen" refers to the portion of abdomen below the umbilicus. Three topographic regions can be identified: the hypogastrium in the middle and the left and right iliac fossa, both located lateral to the hypogastrium, in the left and right inferior part of the surface of the human abdomen, respectively. The majority of men and women will complain, at least once in their life, of a pain localized in the lower abdomen. For this reason, the number of GP's referrals for a lower abdominal pain is expected to be high. A number of different diseases can result in a pain, of variable mode of presentation, intensity, and duration, in the left iliac fossa, the right iliac fossa, and the hypogastrium (this latter also termed "suprapubic pain"), respectively. These may arise from different organs (bowel, lower urinary tract, and female reproductive system) and thus potentially involve different specialists (general surgeon, urologist, and gynecologist). The aim of this chapter is to provide general criteria (essentially based on patient's history and examination) that may lead to suspicion of a urological origin for lower abdominal pain (and the need for a urological referral). The main features for the differential diagnosis with diseases belonging to other apparatus will also be provided in order to lead GPs to make the most appropriate specialist referral.

Hints to Make a Differential Diagnosis of Lower Abdominal Pain

An accurate patient history should focus on the duration and intensity of pain and whether it is a primary presentation or recurrent pain. A thorough examination is crucial to help in localizing the affected organ. It should start with abdominal palpation (looking for palpable masses or signs of peritonism) followed by digital exploration of the inguinal canal in the male and the crural canal in the female. Digital compression of the vertebral spinous processes, the paravertebral muscles, and the pubic tendon of tight adductor muscles may help to identify pain trigger points suggestive of radiculitis.

In males, digital rectal examination of the prostate helps to identify a pain of prostatic origin. In females, vaginal examination should preferably be carried out both manually and with the speculum. Digital examination of the vaginal fornices, the cervix, and the trigone (this latter palpable through the anterior vaginal wall) may help to locate the origin of the pain. Tables 2.1 and 2.2 report the main clinical situations that may present with iliac fossa and hypogastric pain, respectively.

Table 2.1 Most common urological and non-urological diseases that may cause pain in the right or left iliac fossa

Disease	Patient's history and/or symptoms	Examination findings
Ureteric calculi[a]	History of urinary calculi, recent episode of renal colic, dysuria	Severe pain triggered by compression of a localized point of the iliac fossa,[b] microscopic hematuria
Acute appendicitis (right iliac fossa)	Nausea, low-grade fever, history of pain beginning in the periumbilical region and migrating to the right lower quadrant	Right lower quadrant tender during palpation; rebound tenderness, Rovsing's sign (pain in right lower quadrant with palpation of left lower quadrant)
Inguinal hernia	Male, pain exacerbated with standing position, strain, or heavy lifting	Herniation of bowel detectable by digital exploration of the inguinal canal
Sigmoid diverticulosis (left iliac fossa) Cecal perforation (right iliac fossa)	Elderly, irregular bowel habits, recurrent colicky pain	Localized tenderness in either the left or right iliac fossa, palpable mass, abdominal guarding, fever
Extrauterine pregnancy	Absence of period or known pregnancy	Peritonism, signs of shock, positive pregnancy test
Vertebral ovarian pain (ovulation, bleeding, torsion, or rupture of ovarian cyst)	Ovulation, known ovarian cystic disease	Painful palpation of vaginal fornices
Pain referable to a vertebral radiculitis	Pain occurred after an abrupt movement, known vertebral disease	Pain exacerbated by digital compression of the spinous vertebral processes

[a]Occasionally, a calculus that has migrated to the distal portion of the ureter can lead to a severe pain exclusively radiated to the corresponding iliac fossa (in the absence of an accompanying loin/flank pain)

[b]A worsening of the pain following digital compression in the area of the iliac fossa where the ureter crosses the iliac vessels (usually corresponding to the midpoint of a line between the umbilicus and the anterior superior iliac spine) may suggest a ureteral stone

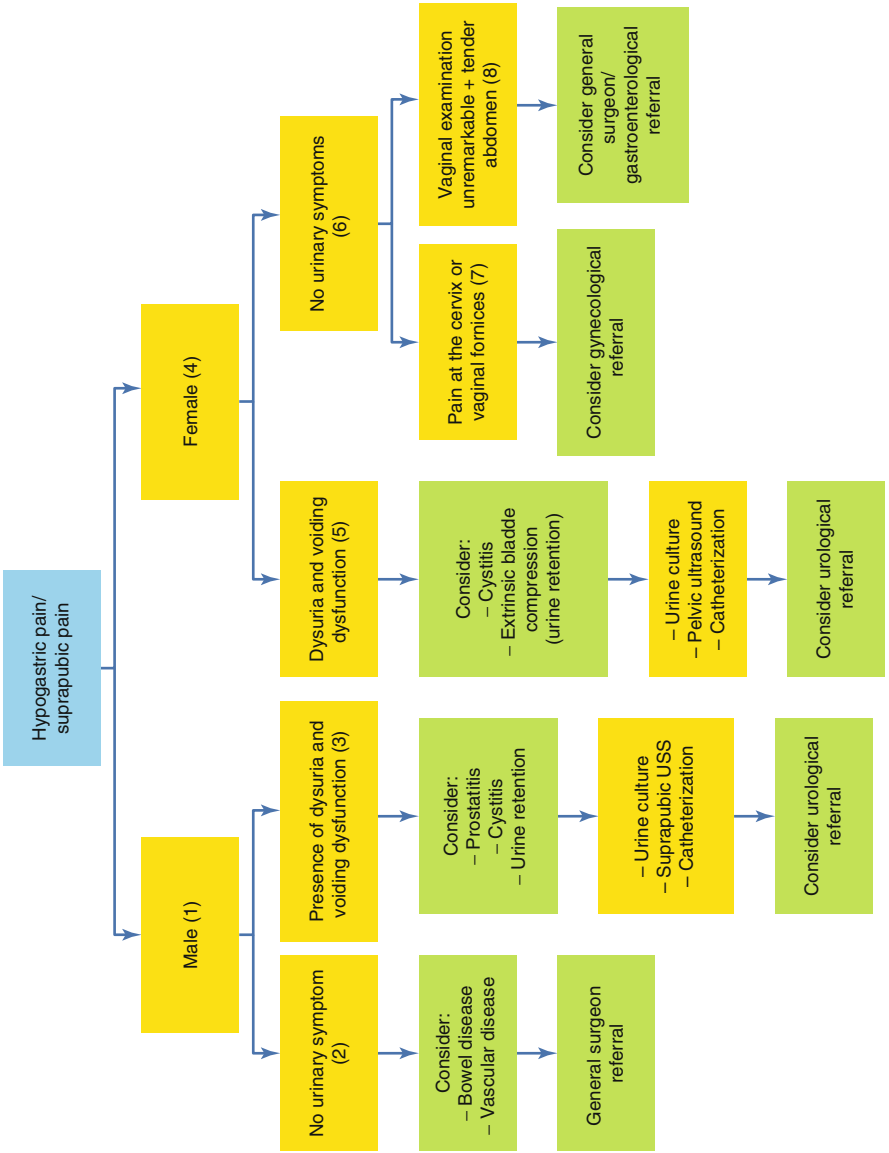
Table 2.2 Most common urological and non-urological diseases that may present with a suprapubic pain

Disease	Patient's history and/or symptoms	Examination findings
Acute or chronic urine retention[a]	Long-standing lower urinary tract symptoms, severe pain, oliguria, or anuria	Palpable suprapubic mass
Acute or chronic prostatitis	Dysuria, urinary frequency, fever in the acute phase. Urinary symptoms can be mild or absent in the chronic phase	Painful, swollen, and hot prostate in the acute phase. Digital rectal examination can be unremarkable in chronic prostatitis
Acute cystitis	Dysuria, urinary frequency	Examination of the anterior vaginal wall can be painful, leukocytes and/or nitrates on urine dipstick
Pelvic inflammatory disease	Young women, unprotected sexual intercourse	Cervical pain on palpation
Endometriosis	Young women, pain exacerbated during period	Cervical pain on palpation
Osteitis pubis	History of inguinal hernia repair or pelvic surgery, athletes, pregnancy	Pressure on the pubic tubercle exacerbates the pain
Irritable bowel disease	Long-term history of intermittent, migrating abdominal pain, anxious temperament, irregular bowel habits	Abdomen thoroughly tender upon examination

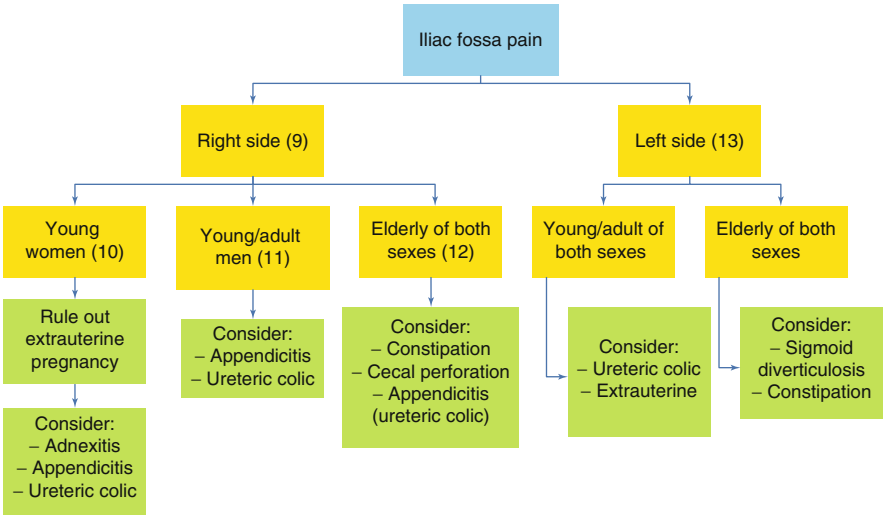
[a]Acute urine retention may occasionally occur in totally asymptomatic patients as a result of a sudden blockage of the urine output due to blood clots or acute prostatitis, although in the majority of cases it represents a complication of an obstructive prostate in patients with lower urinary tract symptoms. Acute urinary retention usually presents in patients with normal or reduced bladder compliance; hence, the patient usually experiences severe hypogastric pain for urine volumes minimally exceeding the normal bladder capacity of 300–400 ml. On the contrary, chronic urinary retention occurs in bladders that have lost their compliance because of a long-standing history of voiding symptoms with high urine residual volumes. The patient usually presents with an enlarged bladder with high urine volume (even 2,000 ml) in spite of only low or moderate discomfort. Overflow incontinence is a frequently associated symptom that describes severe urinary urgency and frequency followed by the emission of only a small amount of urine without resolution of the chronic retention

Algorithm for Managing Hypogastric and Iliac Fossa Pain in the GP's Office

These flowcharts aim to provide the GP with simple suggestions to guide the sometimes difficult decision-making in choosing the most appropriate specialist for referring a patient with hypogastric pain, also referred as "suprapubic pain" (Flowchart 2.1), and iliac fossa pain (Flowchart 2.2).



Flowchart 2.1 Hypogastric pain/suprapubic pain



Flowchart 2.2 Iliac fossa pain

Comments About Flowchart 2.1

1. Diseases causing hypogastric pain/suprapubic pain in a male patient differ in type and frequency of presentation from those affecting a female patient.
2. Absence of associated urinary symptoms should prompt the GP to consider a bowel disease as the most likely explanation of the symptom. In young patients, a history of recurrent and migrating abdominal discomfort, bloating, and modification of bowel habits with alternation of diarrhea and constipation can suggest an irritable bowel syndrome. In patients with vascular risk factors and/or comorbidity, acute hypogastric pain may be the result of dissection of an arterial iliac aneurysm or bowel infarction. If any of these latter conditions are suspected, an referral to an emergency department is mandatory.
3. When hypogastric pain is associated with urinary symptoms, urinary retention must always be ruled out, particularly in elderly patients whose frail mental condition sometimes makes it difficult to interpret their symptoms. The finding of a suprapubic mass during examination of the hypogastrium warrants catheterization to rule out urine retention even if urinary symptoms are mild. When available, suprapubic ultrasound is a simple and noninvasive method to rule out the presence of urine retention. A distended bladder due to chronic urine retention may contain up to 2–3l of urine. In this case, it is mandatory to monitor the patient's urine output for at least 24 hours following catheterization because of the risk of severe polyuria.

 Cystitis or bladder stones are usually accompanied by burning while urinating and urinary frequency. However, the most common cause of suprapubic/hypogastric pain in young and adult males is prostatitis. Urinary symptoms (dysuria and/or frequency and/or urgency), while common, can also be absent.
4. The spectrum of diseases causing hypogastric pain in females differs substantially from that of males.

5. The presence of urinary symptoms such as dysuria, frequency, and urgency is highly suggestive of cystitis. In the case of bacterial cystitis, the urine dipstick is usually positive for leukocytes and/or nitrates, whilst urine culture shows significant growth of a bacterial strain. Antibiotics are usually effective in relieving symptoms and clearing urine. Failure to respond to antibiotic course and/or negative urine culture may indicate so-called "abacterial" cystitis or urethral syndrome. It is important in such cases to rule out the possibility of an extrinsic bladder compression from a pelvic mass or a bladder tumor. Urine retention is far less frequent in females and should prompt the suspicion of a pelvic prolapse or a neoplastic mass (e.g., carcinoma of the cervix).
6. When hypogastric pain is not accompanied by urinary symptoms, the patient's history and examination should aim to look for hints that may help in the differential diagnosis between gynecological and gastroenterological disorders.
7. A careful vaginal exploration may help to suspect a pelvic inflammatory disease in case of tenderness localized at the level of vaginal fornices. An inflammatory process localized to the womb (endometriosis, cervicitis, etc.) has to be suspected when the uterine cervix is painful upon palpation.
8. A lower abdominal pain that is worsened by palpation along with a negative pelvic examination suggests inflammatory bowel diseases. Referral to a general surgeon or gastroenterologist may be appropriate.

Comments About Flowchart 2.2

9. In the differential diagnosis of a right-sided iliac fossa pain, it is important to consider the patient's age and sex.
10. In a fertile female, pregnancy should always be ruled out, particularly in the presence of delayed period, by carrying out a pregnancy test (easily feasible in the office using pregnancy test strips). It should always be kept in mind that a pain in either the two iliac fossae can be the presenting symptom of an extrauterine pregnancy. After pregnancy has been excluded, the following clinical conditions should be considered as the most likely: appendicitis (signs of peritonism helps in the diagnosis), adnexitis (an inflammatory disease affecting the fallopian tubes and ovaries: vaginal exploration is usually painful), and ureteric colic.
11. In young or adult men, ureteric colic and appendicitis are the most likely clinical conditions to included the differential diagnosis.
12. In elderly patients, while appendicitis is always possible, a cecal perforation secondary to a tumor needs to be taken into consideration. A differential diagnosis among these two diseases may be extremely difficult due to overlapping signs. Often, mild symptoms with a palpable mass may simply be due to constipation. Ureteral stones are always possible but less probable than in younger men.
13. When assessing a left-sided iliac fossa pain, it is important to exclude the possibility of sigmoid diverticulitis, not an uncommon situation in elderly patients of both sexes. Sigmoid diverticula are highly prevalent in the elderly and can occasionally undergo inflammation or even perforation resulting in left lower quadrant pain, fever, and the feeling of a palpable mass. Younger adult diseases causing left iliac fossa pain include adnexitis and ectopic pregnancy in females and ureteric colic in both sexes.

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Chapter 3
Swollen and/or Painful Groin

Satvinder Mudan and Ana Belen Fajardo-Puerta

Abstract The groin is where the trunk meets the thigh. The intra-abdominal viscera are separated from somatic structures of the lower limb, yet portals must exist to allow nerves, lymphatics, blood vessels, and other structures to pass to the thigh and genitalia. As with all portals, this predisposes to hernias of various kinds, and inguinal hernia remains the most common cause of groin swelling and the repair of inguinal hernia the most commonly performed operation in general surgical practice. Even so, repair of groin hernia continues to challenge surgeons, thus identifying the complexity of the regional anatomy and the mysteries of function of the anterior abdominal wall, pelvic musculature, and ligaments. Of course, not all swellings in or about the groin are hernias, and this chapter takes an anatomic approach to guide the reader through clinical diagnosis of the soft tissue swellings in the groin arising from the structures present in the region.

Keywords Inguinal • Groin • Hernia • Swelling • Scrotal • Femoral • Varix

Introduction

Groin swelling with or without pain is a common complaint in general practice. The differential diagnosis is diverse, and careful history taking and clinical examination are critical to direct management and direction of further investigations (Table 3.1).

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Table 3.1 Diagnostic sieve of groin swellings

Location	Disease	Clinical features
Skin and subcutaneous tissue	Sebaceous cysts Dermoid cysts Pilonidal cysts	In the skin, irreducible and do not have a cough impulse, if signs of infection drainage is advisable
	Lipoma	Subcutaneous, soft, lobulated, irreducible, and do not have a cough impulse
	Neurofibromata	Multiple, over most of the body and associated with cafe au lait pigmentation
Blood vessels	Femoral artery aneurysm	Pulsatile in all directions. Murmur at auscultation. Often bilateral
	Saphenous varix	Compressible. Disappears on decubitus. Palpable thrill with coughing.
Lymph nodes	Lymphoma	Noncompressible and irreducible, soft rubbery, and usually mobile
	Metastatic	Secondary from malignant melanoma and from pelvic viscera such as anal or vulval cancer, may be hard and fixed
	Inflammatory	Noncompressible, shotty, tender, and sometimes painful Usually bilateral STD: syphilis, lymphogranuloma venereum, gonococcus, herpes simplex, and HIV Infection in the leg: skin infections from minor injury, cat scratch, tinea pedis, and chronic skin conditions such as eczema
Hernia	Localization	Inguinal, usually reducible Direct Medial to inferior epigastric vessels Through Hesselbach's triangle Indirect Lateral to inferior epigastric vessels Through internal ring along spermatic cord Femoral, usually irreducible, emerges through femoral canal, medial to femoral vein and passes from below inguinal ligament upward to the inguinal region
	Complexity	Uncomplicated Reducible hernia: The protruding viscus can be returned to the abdomen on lying down and with gentle pressure Complicated Irreducible (incarcerated) hernia: The protruding viscus cannot be returned to the abdomen Strangulated hernia: the vascularity of the viscus is compromised Occurs more frequently with small orifices and in the indirect hernias

Table 3.1 (continued)

Location	Disease	Clinical features
Primary testicular	Varicocele	No pain. Bag of worms texture
	Hydrocele	Irreducible. No pain. To distinguish, transilluminate (hernias will not light up)
	Testicular torsion	Elevation of testis may aggravate pain; abnormal testicular lie; cremasteric reflex usually absent
	Tumor of the spermatic cord (fibroma)	
	Testicular tumor	Non-tender testicular mass
	Epididymitis	Acute onset. May have symptoms of urinary tract infection. Bacterial origin
	Cryptorchid: undescended testicle	Scrotum does not contain two testes
		The genitalia should be examined for evidence of hypospadias or ambiguity. Prader-Willi, Kallmann's, or Laurence-Moon-Biedl syndromes
Pain with no swelling	Chronic muscle strain or athletic pubalgia (Gilmore's groin)	Adductor strains and osteitis pubis are the most common musculoskeletal causes of groin pain in athletes
		Differential diagnoses with iliopsoas bursitis, stress fractures, avulsion fractures, nerve compression, and snapping hip syndrome
Others	Psoas abscess	Fluctuant, lateral to the femoral vessels, and usually associated with a mass in the iliac fossa
	Nerve tumors	Schwannoma. Very rare
	Cyst of the canal of Nuck	Female. Rare
	Seroma/abscess	Following surgical hernia repair
	Retroperitoneal sarcoma	Rare
	Hematoma	Arising from the retroperitoneum
		Antecedent to trauma
	Ascites	History of cirrhosis or advanced gastrointestinal tumor (malignant ascites)

It is very likely, especially in a man, that an intermittent groin swelling will be an inguinal hernia, and the history alone will direct the doctor to this diagnosis. Clinical examination leads to conclusion of the diagnosis and its classification into type and urgency. Other pathologies might be more vexing and overlap with the hernia diagnosis outside of the typical presentation of the latter. Hernia may be a result of other potentially more serious pathologies, and it remains important to establish a good clinical history that includes the interrogation of obvious symptoms such as site, duration, and pain but also constitutional disturbances such as weight loss, abdominal swelling, and chronic problems of respiration, urination, or bowel movement. Even in the case of obvious groin hernia, examination should always include examination of the abdomen and the chest.

The next most common diagnosis for groin swelling is nodal disease and careful history taking and physical examination to determine the causation of inguinal lymphadenopathy. The inguinocrural lymph nodes drain the perineum, perianal

area, lower abdominal wall, and lower limb. Infection or tumor in any of these regions may produce enlargement of these nodes. It is therefore pertinent in patients presenting with swelling in the groin to always examine the groin in conjunction with the rest of the body and not in isolation and avoid overlooking a serious but treatable diagnosis. Otherwise the diagnostic strategy for a swelling in the groin is an exercise in local anatomy and an understanding of the physical signs of the pathologies that occur in the region: skin, subcutaneous tissue, lymph nodes, femoral blood vessels, long saphenous veins, and the inguinal and femoral canals.

The next pages will take the general practitioner through the diagnostic tree for swelling in the groin.

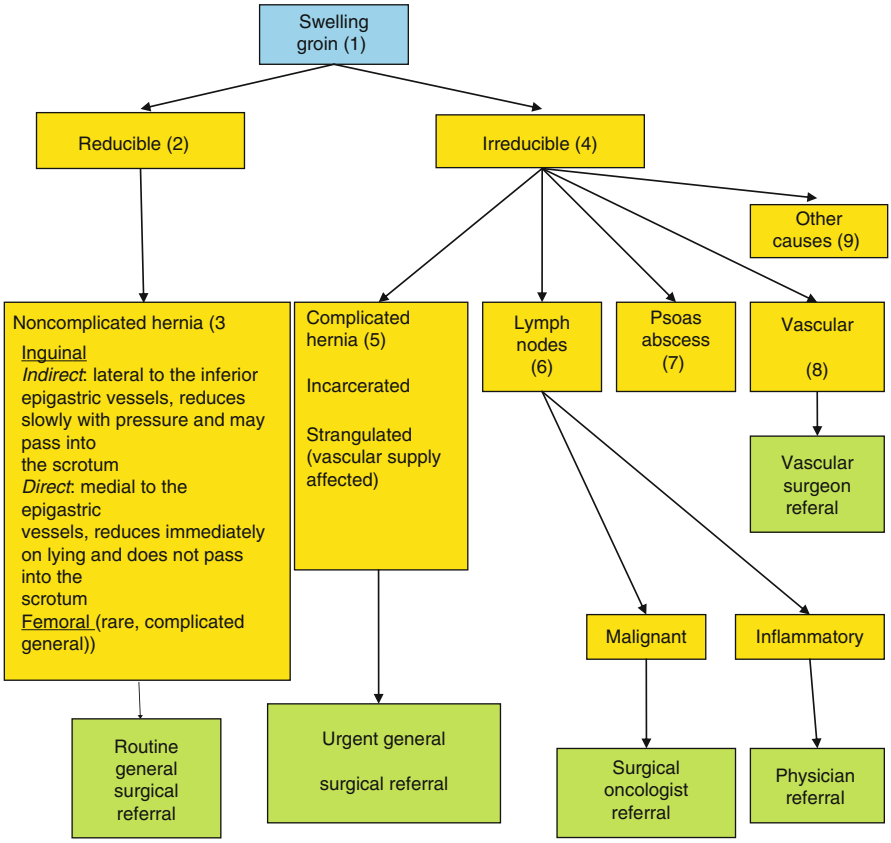
Management of Swollen and/or Painful Groin

Comments About Flowchart 3.1

1. The inguinal area should be examined both with the patient standing and facing the physician and with the patient laying on decubitus. The presence of a discrete bulge that may be accentuated with the Valsalva's maneuver and cough indicates a hernia. The physical findings are sometimes but not always accompanied by a discomfort or dragging sensation in the groin. In the majority of cases, hernia can be diagnosed from the history and clinical examination, but in uncertainty, ultrasonography may be useful in differentiating an hernia from other causes of groin swelling in particular if the swelling does not reduce.
2. Where a reducible swelling is demonstrated and the history and clinical findings point to inguinal hernia, it is common place to attempt to determine whether the hernia is of the direct type or the indirect type as described in the section that immediately follows, indicated by number 3.
3. Hernia in the groin region can arise from the inguinal canal or the femoral canal. It can be considered as the most common condition for which primary care physicians refer patients for surgical management.
 Inguinal hernias are more common by far in both men and women than femoral hernia. Inguinal hernia occurs in men more frequently than in women with a ratio of 20:1. The lifetime risk for a male to need hernia operation is 25 %.

 Femoral hernias are more common in women than in men, and this is said to be because of the differences in pelvic morphology. Hernias come through areas of weakness in the anterior abdominal wall, and in the groin, the areas of weakness are the inguinal canal which in the male transmits the spermatic cord from the retroperitoneum to the scrotum and in the female the round ligament of the uterus to the labia majora. The femoral canal allows for passage of the femoral vessels, femoral nerve, and lymphatics into the upper thigh.

 Condition that weaken the structural integrity of tissues such as increasing age, diabetes, and smoking or result in increased intra-abdominal pressure such as chronic cough and prostatism promote hernia formation. Typically, an uncomplicated inguinal hernia presents as a soft and painless swelling in the groin, although discomfort is not uncommon and the swelling disappears on



Flowchart 3.1 Swelling groin

lying down, and is more obvious when standing or at the end of the day when it may also be more symptomatic. Coughing or staining pushes out the hernia and demonstration of the cough impulse is classically part of the examination of hernia. The herniation may contain extraperitoneal fat or even viscera such as small intestine and less commonly the large bowel or even bladder.

Inguinal hernias fall into two groups. A direct inguinal hernia protrudes directly through a weak and deficient posterior inguinal canal wall medial to the inferior epigastric vessels and is more commonly seen in the elderly male. An indirect inguinal hernia protrudes through a weak and dilated internal or deep inguinal ring and into the inguinal canal, and thus, the hernia origin lies lateral to the inferior epigastric vessels and may be associated with congenital abnormalities like a patent processus vaginalis or abnormalities of testicular decent. For the general practitioner, the difference is academic but the surgeon might plan the operative strategy slightly differently, depending of the type. Clinical examination to distinguish the two is not reliable.

4. When the swelling is not reducible, the differential diagnosis is much wider. In general practice, a complicated hernia where the content cannot be returned to

the body cavity is still the most common cause of an irreducible groin swelling, but the many other causes described in Sects. 5–9 need consideration. As ever, the clinical history remains critical, and here, imaging either by ultrasound or CT scan is likely to be necessary.

5. An hernia might be complicated by incarceration where the hernia contents will not reduce and the swelling is persistent. As a broad generalization, a wide-necked hernia that reduces easily is unlikely to incarcerate, and so the potential for serious complications of hernia such as strangulation are uncommon, whereas a small tight hernia might lead to incarceration of a segment of bowel or a part of the wall (Richter's hernia); the latter may well present in a more insidious way until the trapped bowel wall becomes ischemic and perforation ensues, leading to a more profound picture of acute abdomen and systemic disturbance. An hernia complicated by incarceration should be dealt with expeditiously, and if there is pain and tenderness over the swelling or colicy abdominal pain, then emergency operation must be considered for fear of strangulation of the hernia contents. Femoral hernia do not usually have a cough impulse, and the hernia protrudes forward through the saphenous opening and then, because of the deep fascia of the thigh, turns upward to the groin. Femoral hernias have a high risk of incarceration or strangulation, and often the expected signs and symptoms of strangulation are not present until late. Femoral hernia should always be repaired expeditiously.
6. Lymph nodes are usually multiple, mobile, not compressible, and have no cough impulse. More chronically enlarged nodes may show a degree of deep fixation and be described as "matted." In some cases, an abscess can be developed with tender fluctuant swelling in the groin and eventually pus discharge. Inguinal lymphadenopathy might arise from:

 Malignancy:

 Primary Lymphoma: other superficial nodal basins such as the axillae and the neck should be examined, and inquiry made for systemic symptoms of fever, night sweats, fatigue, and weight loss. Full imaging by CT scan from the neck to the groins is needed, and node biopsy will be needed. The nodes are large, soft, mobile, and rubbery to feel.

 Metastatic: secondary from cutaneous melanoma of the lower limb and less commonly squamous carcinoma of anus, vulva, or lower third of vagina. The nodes are large, hard, and may show fixity.

 Inflammation:

 Sexually transmitted diseases: syphilis, lymphogranuloma venereum, gonococcus, herpes simplex, and HIV.

 Infections in the leg: skin infections from minor injury, cat scratch fever (toxoplasmosis), tinea pedis, and chronic skin conditions such as eczema. These nodes are often small and described as "shotty."
7. Although an uncommon diagnosis psoas abscess presents with a fluctuant swelling in the groin and typically is associated with swelling in the iliac fossa. Imaging by CT will be necessary to demonstrate the problem. The causation can be Crohn's disease or tuberculous disease of the spine.

8. The inguinal region transmits the femoral artery, vein, and nerve from the pelvis into the upper thigh, the crural region of the groin. A pulsatile and expansible swelling sometimes bilateral and exhibiting a murmur at auscultation indicates a femoral artery aneurysm. Other history or evidence of peripheral vascular disease may be present. A saphenous varix is a dilatation or varicosity of the junction of the long saphenous vein with the femoral vein and presents as a compressible swelling with a palpable thrill with coughing. Ultrasound imaging for these conditions is diagnostic, and referral to a vascular surgeon can be made.
9. Less common irreducible swellings in the groin should be separated common cutaneous lesions such as sebaceous (epidermoid) cyst and subcutaneous lipoma, neither of which should represent a diagnostic challenge and do not require any specific imaging. Other soft tissue swellings are more challenging, and sometimes a testicular or scrotal swelling can be confused with a groin swelling.

An undescended testis or ectopic testis may be found and will have a corresponding lack of testis in the scrotum, and its presence confirmed by inguinal ultrasound. Other difficult pathologies include soft tissue swelling of a neoplastic etiology such as tumors of nerve like schwannoma or fibromatosis of the groin. CT scan and, in the case of the latter, biopsy will be needed.

Having a clear understanding of scrotal anatomy allows the examiner to accurately identify most scrotal lesions that may cause swelling demonstrable in the groin. Benign lesions such as hydroceles and varicoceles of the cord are often found incidentally. Epididymitis is bacterial in origin and diagnosed on physical examination by tenderness of the cord, and treated with antibiotics. Testicular swelling may be caused by orchitis, cancer, or testicular torsion. Orchitis is usually viral in origin, subacute in onset, and may be accompanied by systemic illness. Testicular carcinomas are more gradual in onset; the testis will be non-tender on examination. Testicular torsion has an acute onset, often with no antecedent trauma; the involved testis may be retracted and palpably rotated, and will be tender on examination. The swollen testis is always a true emergency. Although history and examination may suggest the diagnosis, testicular torsion can be reliably confirmed only with color Doppler ultrasonography, which must be obtained immediately. If torsion is suspected, surgical consultation should be obtained concurrently with ultrasonography, because the ability to successfully salvage the affected testis declines dramatically after 6 h of torsion.

The most common reason for groin pain without a palpable hernia is a chronic muscle strain. Usually, the groin exploration for patients will likely make the situation worse.

Conclusions

Swelling groin is very common in general practice. Hernia and lymph node enlargement are the most common causes, but this swelling may be part of a generalized disease.

Being systematic with the past medical history, the general clinical examination, and avoiding examination of the groin in isolation are crucial for a good differential diagnose.

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Chapter 4
Swollen and/or Painful Scrotum

Marco Oderda and Paolo Gontero

Abstract Medical conditions affecting the scrotum may present themselves with pain without any sign of swelling, with a painful swelling, or with a painless swollen scrotum. A sudden onset of a scrotal pain or swelling is defined as "acute scrotum" and can have a variety of causes. The diagnostic process is essential to rule out conditions that prompt urgent hospital referral. Among the causes of a painful and swollen scrotum, testicular torsion is the most feared one, as the likelihood of testicular salvage decreases as ischemia increases. Several conditions can mimic testicular torsion, such as torsion of testicular appendages, epididymitis, epididymo-orchitis, trauma, varicocele, inguinal hernia, and even systemic disease, like the rare Schonlein-Henoch purpura. Besides, several conditions can cause painless scrotal swelling. Among these, a testicular cancer must always be suspected when a firm mass is discovered within the testicular parenchyma. The aim of this chapter is to provide a practical flowchart to assist the physician in decision making among the most important scrotal diseases, guiding the choice between an urgent hospital referral and conservative management.

Keywords Acute scrotum • Scrotal mass • Testicular cancer • Epididymitis • Testicular torsion • Varicocele • Hydrocele

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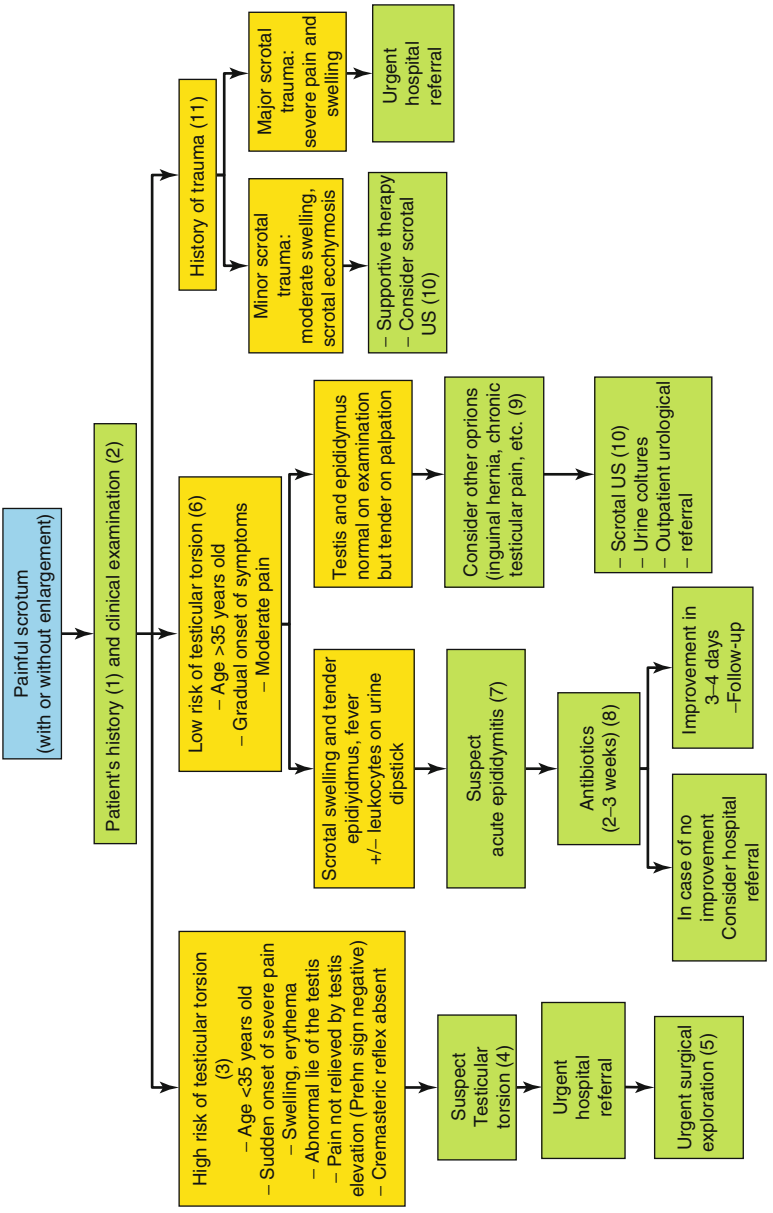
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Introduction

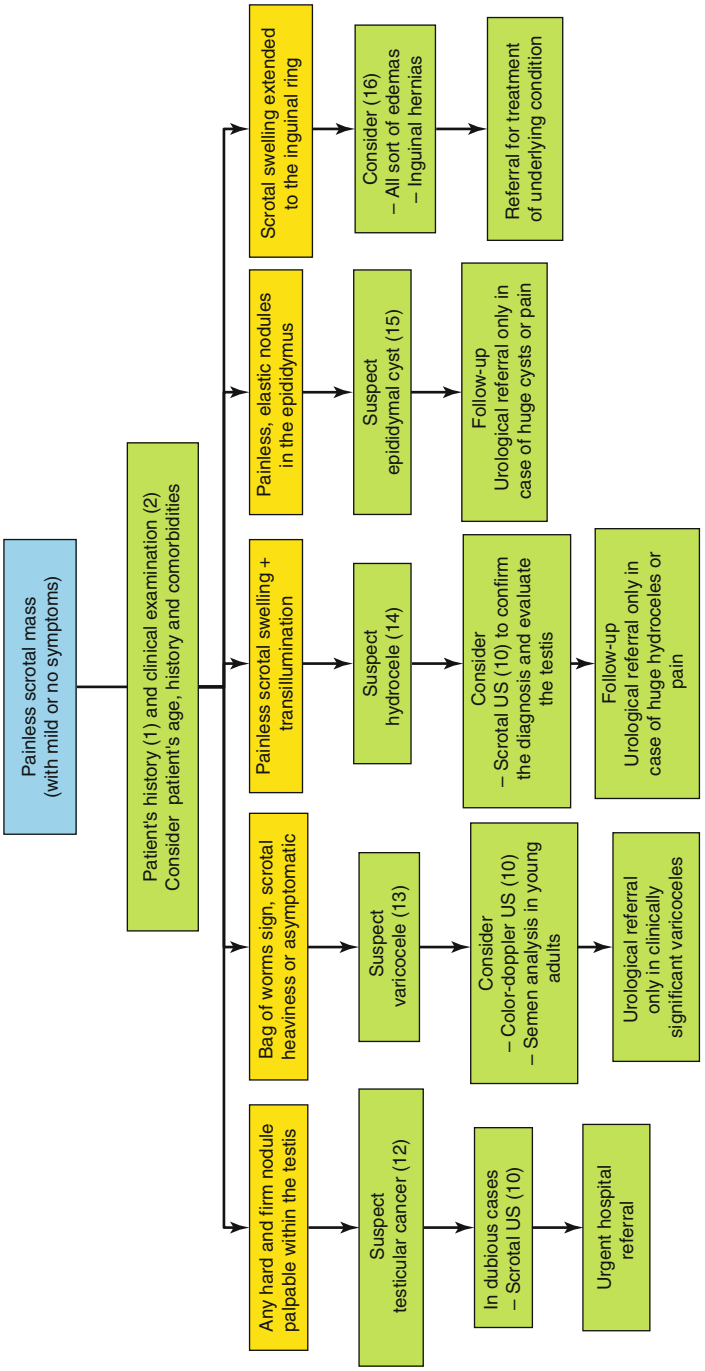
Medical conditions affecting the scrotum may present themselves with pain without any sign of swelling, with a painful swelling, or with both pain and swelling. A sudden onset of a scrotal pain or swelling is a condition defined as "acute scrotum" and can have a variety of causes. Among these, a testicular torsion is the most feared one and represents a urological emergency, as the likelihood of testicular salvage diminishes with the duration of the ischemia. Therefore, the physician has to promptly recognize this condition in any patient presenting with an acute scrotum and request an urgent referral to hospital. Several other conditions can mimic testicular torsion by presenting with scrotal pain and swelling of various degrees, such as torsion of testicular appendages, epididymitis, epididymo-orchitis, trauma, varicocele, inguinal hernia, and even systemic disease, like the rare Schonlein-Henoch purpura. These conditions generally do not require immediate surgical intervention and can be managed at leisure. A careful history and a thorough physical examination allows a diagnosis in most of cases. However, if any doubt about testicular torsion exists, it is advisable to send the patient to the hospital. Sometimes, even a painless scrotal mass can represent an equally urgent condition, being a sign of testicular cancer. Therefore, when dealing with scrotal pain or swelling, the general physician needs to be able to discriminate the real "scrotal emergencies" that need urgent urological referral. The aim of this chapter is to provide a practical flowchart to assist the physician in decision making among the most important scrotal diseases. These will be divided into two main categories: painful scrotum with or without enlargement, addressed in Flowchart 4.1, and scrotal mass with mild or no symptoms, which will be the subject of Flowchart 4.2.

Comments About Flowcharts 4.1 and 4.2

1. A careful history together with an accurate physical exam, can significantly narrow the differential diagnosis of a painful or swollen scrotum. The most common causes of a painful scrotum are reported in Table 4.1. Diseases mostly presenting with a painless scrotal mass are shown in Table 4.2. The age of the patient is important, as testicular torsion is more common in adolescents. Torsion of a testicular appendage or Schonlein-Henoch purpura typically occurs in the prepubertal boys, while epididymo-orchitis usually affects postpubertal boys. Many patients with torsion describe similar episodes of pain in the past that lasted only a short time and resolved spontaneously. A history of trauma does not exclude a testicular torsion: severe pain that persists for more than 1 h after scrotal trauma prompts investigations in order to rule out a testicular rupture or a concurrent acute torsion. Furthermore, the physician has to seek predisposing conditions for urinary tract infections, in particular lower urinary tract symptoms due to obstruction in the elderly or sexually transmitted diseases in younger patients.



Flowchart 4.1 Painful scrotum (with or without enlargement)



Flowchart 4.2 Painless scrotal mass (with mild or no symptoms)

Table 4.1 Common causes of painful scrotum (with or without enlargement)

Pathology	Physical examination	Ultrasound findings	Management
Testicular torsion (4)	Severe pain, swelling, and tenderness. Abnormal lie of the testis, which may be asymmetric ("high-riding" testis). Prehn sign is negative (the lifting of the testicle does not relieve the pain of torsion); cremasteric reflex may be absent (stroking the skin of the inner thigh does not evoke contraction of the cremasteric muscle which should pull up the ipsilateral testis)	Normal parenchyma	Urgent hospital referral. Surgical exploration is mandatory there is suspicion of testicular torsion
Epididymitis (7)	Severe/moderate pain, acute or progressive onset. Swelling and tenderness. Fever, dysuria, and urethral discharge may be present. Prehn sign positive (the lifting of the testicle relieves the pain of the epididymitis)	Heterogeneous parenchyma	Antibiotic therapy. First-line antibiotics are fluoroquinolones and cephalosporins, alone or in combination. Hospital referral in most severe cases
Chronic testicular pain (9)	Scrotal pain in absence of testicular and epididymal abnormalities	Normal parenchyma	Consider anti-inflammatory agents. Outpatient urological referral
Inguinal hernia (9)	Groin swelling. Acute pain in case of incarcerated/strangulated hernia	Hernia sac	Referral to general surgeons
Testicular trauma (10)	Severe pain, swelling, tenderness, ecchymosis. Hematocele may be present. History of trauma is essential	Heterogeneous parenchyma; lacerations of the albuginea may be present	Urgent hospital referral, according to the severity of trauma

Table 4.2 Common causes of painless scrotal mass

Pathology	Physical examination	Ultrasound findings	Management
Testicular cancer (12)	Painless testicular mass. Hard and firm nodule within testicular parenchyma	Heterogeneous, usually hypoechoic, testicular mass	Urgent hospital referral
Varicocele (13)	Asymptomatic or mild discomfort. "Bag of worms" palpable	Normal parenchyma	Follow-up. Urological referral only in clinically significant varicoceles
Hydrocele (14)	Painless scrotal swelling. Diagnosis with transillumination	Normal parenchyma. Fluid without echoes	Follow-up. Urological referral only in huge hydroceles or pain
Epididymis cysts (15)	Painless, elastic nodules within the epididymis	Normal parenchyma. Epididymis cysts. Fluid without echoes	Follow-up. Urological referral only in case of huge cysts or pain
Scrotal edema (16)	Painless scrotal swelling	Normal parenchyma	Treat underlying condition

2. The severity of the pain can be often assessed by simply observing the patient. A testicular torsion usually causes a severe pain that is not eased by resting as opposed to the pain due to epididymitis or orchitis that improves in the supine position. Physical examination should start with a general abdominal examination. Renal colic may mimic an acute scrotum due to its radiation to the groin and the scrotum. The inguinal regions must be inspected, seeking for hernias or swelling. The spermatic cord in the groin can be swollen and tender in a patient with epididymitis. The genitalia must be inspected, evaluating discrepancies between the size of the testes, degree of swelling, presence of erythema, and thickening of the scrotal skin. A testicle that has undergone torsion usually is swollen and tender and occupies a high and asymmetric position in the scrotum ("high-riding" testicle). The elevation of the testis elicits the *Prehn sign*: the lifting of the testicle relieves the pain in case of epididymitis (Prehn sign positive), but not the pain caused by acute torsion (Prehn sign negative). The *cremasteric reflex* must also be assessed by stroking the skin of the superior and inner thigh: the normal response is a unilateral contraction of the cremaster muscle that pulls up the scrotum and the ipsilateral testis. This reflex may be absent in a testicular torsion. Tenderness limited to the upper pole of the testis suggests torsion of a testicular appendage, especially when a firm and tender nodule is palpable in this region. Sometimes, a blue dot sign can be visible through the skin, corresponding to a torted, ischemic appendage. A unilateral scrotal swelling without skin changes, usually painless, suggests the presence of a hydrocele. The classic sign of a varicocele, is the scrotal "bag of worms," due to the dilatation of the veins within and surrounding the spermatic cord. In this case, the scrotal swelling becomes particularly evident in the standing position, while it usually decreases in the supine position. The epididymis shows tenderness and induration in early epididymitis; if the testis becomes involved too, the degree of swelling and pain may make palpation no longer possible. Testicular palpation is also essential in the differential diagnosis of a testicular cancer: while a nodule in the epididymis context is usually harmless, and usually relates to a cyst or previous inflammation, the discovery of a painless palpable lump arising from the testicle must arouse the suspicion of a testicular cancer.
3. Testicular torsion is usually seen in young patients, typically <35 years, presenting with acute testicular pain, sometimes associated to nausea and vomiting. The affected testis is usually swollen, tender, asymmetric, and high riding. Prehn's sign is negative and the cremasteric reflex may be absent. Swelling and a coexisting hydrocele may prevent testicular palpation. The patient needs to be urgently referred to the hospital.
4. Testicular torsion has to be considered a urological emergency. The testis has good chances of being preserved if untwisted within 6 h. Testicles that lack normal attachment to the tunica vaginalis and hang free in the scrotum (so-called "bell clapper" testes) are more likely to undergo torsion. Sometimes, the pain can be due to the torsion of a testicular appendage: the appendix testis, a remnant of the Mullerian duct situated in the upper pole of the testicle, is the most common testicular appendage susceptible to torsion. The epididymal appendix, a remnant of the Wolffian duct, is also susceptible to torsion. In both cases, symptoms at presentation are the

same as for testicular torsion, but the onset is generally more gradual. Patients are most often adolescents, presenting with testicular pain. Sometimes, before swelling has developed, it is possible to palpate a small tender area on the upper pole of the testis, corresponding to the twisted appendage. It may even be visible as the "blue dot sign," a small bluish discoloration of the scrotal skin pathognomonic for appendicular torsion. The differential diagnosis with testicular torsion can be very difficult, because of the swelling and the pain that can involve the corresponding scrotal portion. Therefore, all these cases warrant urgent hospital referral. If the diagnosis remains uncertain, especially when edema makes physical examination impossible, surgical exploration is mandatory to assess the viability of the testis.

5. Urgent surgical exploration is prompted without imaging studies in the suspicion of torsion, as any delay in treatment could jeopardize testicular preservation. Therefore, these patients have to be referred urgently to the hospital. Manual detorsion could be attempted, rotating the testis outward.
6. Low risk of testicular torsion includes patients >35 years old, presenting with moderate pain and/or gradual onset of symptoms. Testicular torsion, though less probable, must always be ruled out.
7. Epididymitis can be associated with sexual activity, especially in the young adults, whereas in older patients it is often related to urinary tract infections and prostatitis. In prepubertal boys, congenital anomalies of the genitourinary tract must always be ruled out with voiding cystourethrography. Acute epididymitis usually manifests itself with sudden-onset, painful swelling of the scrotum and the spermatic cord. Sometimes the onset is more gradual and can be accompanied by dysuria, urinary frequency, or urethral discharge. The epididymis is swollen, tender, and painful. Scrotal erythema may develop, together with edema. The ipsilateral testis may be involved, producing epididymo-orchitis and making it impossible to distinguish the testis from the epididymis. Fever may be present. In young patients, the differential diagnosis may be difficult in acute onset cases. Generally, Prehn's sign is positive, since the pain is relieved by elevating the scrotum toward the abdomen, contrary to what happens in testicular torsion. Sometimes, however, inflammation and torsion are seen together: the possibility of a concomitant testicular torsion must always be kept in mind. After acute inflammation has resolved, a fibrotic scar can be palpated as a painless and firm scrotal mass that must not be confused with a testicular malignancy. It should be kept in mind, though, that as many as 10 % of patients with testicular cancer may present with epididymitis.
8. Although it is advisable to send urine sample for culture, antibiotic therapy should be started promptly on empirical basis, without waiting for the results. First-line antibiotics are represented by fluoroquinolones, preferably those active against *Chlamydia*, and cephalosporins, because of their broad antibacterial spectrum. In most severe cases, the combination of the two can be adopted. Antibiotic therapy must be prolonged for 2–3 weeks. Supportive therapy consists of bed rest, up positioning of the testes, and anti-inflammatory therapy. Improvement in local symptoms and fever resolution within 3–4 days indicates treatment response. Persistence of symptoms despite antibiotic therapy warrants hospital referral. In such cases, scrotal US must be useful, chiefly to rule out scrotal abscesses.

9. Other causes of painful scrotum include inguinal hernias, dermatological lesions, and inflammatory vasculitis, together with chronic testicular pain. An inguinal hernia can be suspected in case of groin swelling. It can be palpated inserting a finger in the external inguinal ring. An incarcerated or strangulated hernia provokes acute pain, is not reducible, and requires urgent surgical intervention. Henoch-Schonlein syndrome is a systemic vasculitis that causes purpura, arthralgia, gastrointestinal symptoms, and glomerulonephritis. The scrotum may rarely be involved, with acute pain, tenderness, and erythema. Scrotal involvement is usually self-limiting; therefore, urological consultation is generally not necessary if the primary diagnosis has already been made by the dermatologist. Finally, referred pain to the scrotum can derive from several pathologies, such as an inflamed retrocecal appendix, a ruptured abdominal aortic aneurysm, or renal colic. Chronic testicular pain, due to radicular compression, inflammation of the genitofemoral nerve, or unknown etiologies, is another bothersome cause of a painful scrotum. It is mostly a diagnosis that is made when all other causes of a painful scrotum have been excluded. It is often difficult to manage and usually poorly controlled by painkillers. Referral to a pain clinic should be taken into consideration.
10. While testicular ultrasound (US) is usually accurate in correctly diagnosing most scrotal masses, it cannot be recommended to rule out a testicular torsion. Even when assisted with a vascular evaluation using color Doppler modality, US could generate misleading results since the early phase of a testicular torsion can be associated to an increased vascularity due to blood congestion that could be confused with an infection. On the contrary, when a testicular torsion has been excluded, scrotal US can help in the diagnosis of epididymis or testicular infection and to rule out a scrotal abscess. Furthermore, it is highly sensitive in detecting solid testicular masses or extratesticular masses such as hydrocele, varicocele, or epididymal cysts. It can also exclude lacerations of the albuginea (the fibrous layer surrounding the testicular parenchyma) in cases of moderate testicular trauma. It is usually easily accessible and cost-effective.
11. Testicular injuries can result from either a blunt or, more rarely, penetrating trauma. A spectrum of injuries can occur, from the contusion to the laceration of the tunica albuginea up to the complete testicular destruction or avulsion. Testicular rupture may occur in 50 % of blunt scrotal traumas, especially under intense compression of the testis against the pubic bones. In the suspicion of testicular rupture, an ultrasound can be performed to evaluate the integrity of the tunica albuginea. A color Doppler study can provide useful information on the status of the testicular vascularization, particularly in the rare occurrence of intratesticular hematoma, where bleeding in presence of an intact tunica albuginea compresses the testicular parenchyma, thus mimicking an acute scrotum. Moderate to severe testicular traumas are usually best managed by an A&E referral where a surgical scrotal exploration allows a correct diagnosis, drainage of the hematoma, and repair of the injury or removal of the testicle in case of major disruption. Minor scrotal hematoma, so-called hematocele, a situation that indicates a collection of blood within the tunica vaginalis of the testicle, can usually be managed conservatively, with ice packs and oral painkillers.

12. Any solid mass arising from the testis and confirmed at ultrasound has to be considered a testicular cancer until otherwise proven, because of the rapid risk of progression and metastatic potential of the majority of testicular malignancies. Therefore, urgent urologic referral is mandatory. Although rare (1–1.5 % of all cancers in the male), testicular cancer represents the most common solid tumor of young adult males. Only 1–2 % of cases are bilateral at diagnosis. 90–95 % of primary testicular tumors are germ cell tumors, comprising seminoma (35 %) and non-seminomatous germ cell tumors (NSGCT), such as yolk sac tumor (20 %), teratoma (5 %), and choriocarcinoma (<1 %). The remaining 5–10 % is made up of stromal testis tumors, which mostly exhibit benign behavior. The incidence peak is around 30 years for seminomatous and around 40 years for non-seminomatous neoplasms. Men complaining of a testicular mass in their 50s are more likely to have a lymphoma. Testicular cancer usually presents as a painless, firm nodule incidentally discovered within the testicle. Sometimes inflammation or a reactive hydrocele may coexist. A hard, firm mass in the testicular parenchyma can be easily felt at palpation. Ultrasound will reveal a heterogeneous, usually hypoechoic testicular mass. Since testicular tumors tend to grow rapidly, any suspicious nodule within the testicle should be urgently referred to the urologist to carry out surgical exploration. Before undergoing explorative surgery in the suspicion of a testicular cancer, it is useful to assay serum alpha-fetoprotein, beta HCG, and LDH, which may be elevated in several types of testicular cancers. These have both diagnostic and prognostic usefullness. Seminomas tend to have a better prognosis than non-seminomas, the latter are more aggressive with a higher propensity to metastasize. Testicular cancers are very sensitive to both radiotherapy and chemotherapy with a very high chance (90 %) of cure even when metastatic. Table 4.3 summarizes the main prognostic and therapeutic information of testicular cancers, according to the disease stage.
13. Varicocele is caused by a dilatation of the pampiniform plexus of the veins within and surrounding the spermatic cord. It can cause mild discomfort or remain completely asymptomatic. According to different grades of severity, varicocele can be visible only on ultrasound (grade 1), palpable on Valsalva maneuver (grade 2), palpable at rest (grade 3), or macroscopically visible (grade 4). The pathognomonic sign is the palpation of the so-called bag of worms, refering to the vermiform appearance of the dilated veins above a normal testis and epididymis. Color Doppler ultrasound confirms the diagnosis and evaluates the grade of the varicocele. The patient has to be reassured if the varicocele is not clinically significant. Urological referral is prudent in grades 3 and 4, because of the potential detrimental effect on fertility. The execution of a semen analysis is recommended in these cases, in young adults potentially seeking children. Treatment is offered in presence of clinically significant varicocele together with abnormalities in semen analysis, infertility, or testicular growth retardation in adolescents. It consists of the surgical ligature or embolization of the spermatic veins.

Table 4.3 Treatment options and prognosis of testicular cancer (seminoma and non-seminomatous germ cell tumors, NSGCT) by pathologic stage as defined by TNM classification

Stage	TNM stage	Explanation of TNM	Treatment options by type	5 years survival probability (%)
I	T1–T4, N0, M0 stage	Tumor confined to the testis, with no evidence of extratesticular localizations	*Seminoma*: orchidectomy followed by active surveillance/or adjuvant chemotherapy/or adjuvant radiotherapy	Around 100
			NSGCT: orchidectomy followed by active surveillance/or adjuvant chemotherapy/or surgery (retroperitoneal lymphadenectomy)	Around 100
II	N+ stage	Tumor with evidence of metastases to retroperitoneal lymph nodes	*Seminoma*: orchidectomy followed by radiotherapy/or chemotherapy	Almost 100
			NSGCT: orchidectomy followed by retroperitoneal lymphadenectomy/or chemotherapy/or both	98–100
III	M+ stage	Tumor with metastases to supradiaphragmatic lymph nodes or distant metastases	*Seminoma*: orchidectomy and primary chemotherapy.	72–86
			NSGCT: orchidectomy and primary chemotherapy, followed by debulking surgery when possible	48–92

14. Hydrocele consists of a collection of fluid within the tunica vaginalis, which surrounds the testis. It can be congenital or acquired after trauma, epididymitis, testicular torsion, or tumors. It often presents as a painless swelling of the scrotum which transilluminates, confirming the presence of liquid in the scrotum. Patients have to be reassured. Treatment is advised only if hydrocele reaches a significant size.
15. Epididymal cyst is a benign condition consisting of a dilatation of an epididymal tubule. It usually appears as a rounded, painless, elastic nodule, easily palpable above the testicle. It is commonly seen in middle-aged patients. Size can vary from few millimeters up to several centimeters. Ultrasound examination is only required in uncertain cases. The content usually consists of clear fluid; sometimes sperms can be retrieved within an epididymal cyst. Treatment, which consists of surgical removal, should be offered only for large symptomatic cysts. Patients have to be reassured about the benign nature of this kind of lesions and followed.
16. Other causes of painless scrotal masses include all sorts of scrotal edemas, inguinal hernias, and sebaceous cysts of the scrotum. Acute scrotal edema is a condition characterized by sudden collection of fluid in the scrotum. Some cases are secondary to congestive heart failure, while the majority are idiopathic. Squeezing of the edematous fluid out of the scrotum allows the physician to carefully palpate the testis and the scrotum, looking for signs of inflammation or other anomalies.

Conclusions

When dealing with testicular pathologies, the general physician must differentiate the conditions that require urgent hospital referral from those that can be conservatively managed. Among the causes of painful and swollen scrotum, testicular torsion is the most feared one, being a real urological emergency. Suspicion of a twisted testicle must prompt hospital referral, especially in a young patient. Epididymitis represents the most common disease that may lead to misdiagnosing a testicular torsion. Epididymitis can be managed with more leisure but needs appropriate and timely antibiotic therapy, especially in young adults beacuse of a risk of infertility. Among the causes of painless scrotal masses, testicular cancer must always be ruled out: any mass found within testicular parenchyma warrants urgent hospital referral. Once these real emergencies have been excluded, a broad spectrum of other diseases must be considered in the differential diagnosis of a scrotal mass. Careful history taking and a thorough clinical examination are essential in the diagnostic process and will guide the general physician to correctly refer to which specialist.

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Chapter 5
Empty Scrotum

Matthew S. Christman and Douglas A. Canning

Abstract The empty scrotum can indicate a range of disorders, from primary cryptorchidism (a.k.a. an undescended testicle, UDT) to disorders of sexual differentiation (DSD). UDTs are identified in approximately 2–4 % of full-term newborn boys and account for one of the most common congenital anomalies encountered by both the pediatrician and urologist. On the other hand, DSD encompass a variety of rare and complicated disease processes that afflict the child with ambiguous genitalia. While the true incidence of DSD can be difficult to ascertain, it has been estimated to be present in 2.2 per 10,000 births. Both genetic and environmental factors may be involved in the pathogenesis of each of these diagnoses. For the child to receive proper care, it is critical that the primary care physician/pediatrician recognize these disorders and perform thorough evaluations of the empty scrotum. Urologists play a large role in the overall care of these patients and decisions regarding surgical intervention. In this chapter, we aim to outline the steps in the evaluation and diagnosis of the empty scrotum as well as to provide some guidance on the decision of when to refer the child for specialty care.

Keywords Empty scrotum • Cryptorchidism • Undescended testicle • Disorders of sexual differentiation • Ambiguous genitalia

Introduction

A spectrum of disorders can result in the varied phenotypic expression of an empty scrotum, from the more commonly encountered cryptorchidism to the more rare disorders of sexual differentiation (DSD). Cryptorchidism translates to “hidden testis”

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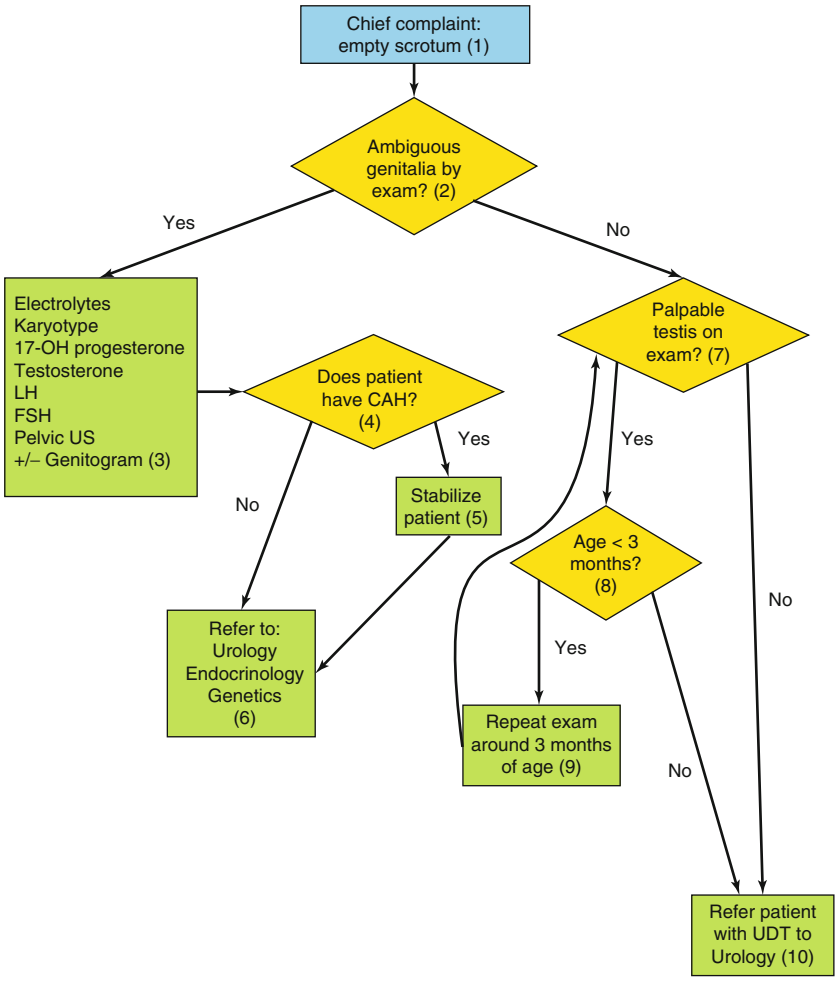
and may be substituted with the term “undescended testicle/testicles” (UDT). UDTs are identified in approximately 2–4 % of full-term newborn boys and account for one of the most common congenital anomalies encountered by both the pediatrician and urologist. On the other hand, DSD encompass a variety of rare and complicated disease processes that afflict the child with ambiguous genitalia. While the true incidence of DSD can be difficult to ascertain, it has been estimated to be present in 2.2 per 10,000 births. Both genetic and environmental factors may be involved in the pathogenesis of each of these categories of diagnosis. Proper characterization of the patient with an empty scrotum is critical to ultimately determining treatment.

Management of Empty Scrotum

Comments About Flowchart 5.1

1. Evaluation of the empty scrotum begins with a good history. The differential diagnosis encompasses a variety of disease processes (Table 5.1). Determining the age of presentation and whether or not a testis has been seen or palpated within the scrotum previously can help potentially differentiate a UDT from a retractile testis from one that has ascended. UDTs are known to be more common in low birth weight, premature infants, with an incidence of up to 45 %. It is also important to elucidate surgical history, as a prior history of ipsilateral hernia repair or orchiopexy could suggest secondary cryptorchidism, testicular retraction, or postoperative testicular atrophy. Furthermore, a history of discordant karyotypes between an amniocentesis and an infant karyotype should raise concern for the patient with ambiguous genitalia. Family history of infertility, amenorrhea, and infant mortality can also provide pertinent information. Various syndromes have been associated with both cryptorchidism and ambiguous genitalia.
2. Examination for the testis should be conducted with the patient in the supine position. For older boys, additional examination in the upright cross-legged, standing, and/or squatting positions can help to overcome the cremasteric reflex. During examination of the scrotum, pressure should be applied along the ipsilateral inguinal canal with one hand while simultaneously palpating for the testicle with the opposite hand. This can close the internal ring to prevent sliding of the testicle. In some situations, liquid soap or lubricating jelly can be used to allow an examining hand to slide over the groin to augment the ability to palpate the underlying testicle. The presence of a hypoplastic scrotum, versus one that is well formed with rugae, can increase suspicion of a UDT. The examiner should also note any asymmetry or mass in the inguinal region which may suggest a hernia. A testis with its midpoint located at or below the mid-scrotum is considered to be in a normal scrotal position.

 A penile exam is critical for these patients as well. Penile length and girth should be noted. A full-term infant with a penis less than 1.9 cm in length should raise suspicion for micropenis and may indicate a diagnosis of DSD. The presence of hypospadias and the position of the urethral meatus should also be noted.



Flowchart 5.1 Empty scrotum

For routine examinations, the prepuce should not be forcibly retracted; this will generally occur naturally by the age of 4 years. Furthermore, the urethral meatus is rarely abnormal if the child has a fully formed and circumferential foreskin.

The presence of ambiguous genitalia is determined based on the physical exam findings and requires immediate evaluation in the newborn. Suspicion may be increased based on bilateral nonpalpable testes, hypospadias (particularly proximal), and micropenis. Together, these findings may indicate a more global abnormality. Hypospadias can be found in up to 12–24 % of patients with cryptorchidism, and chromosomal abnormalities may be found in approximately one-third of patients with cryptorchidism and associated proximal hypospadias.

3. The infant with ambiguous genitalia needs immediate evaluation. A "male" newborn with ambiguous genitalia and an empty scrotum may actually be a genotypic

Table 5.1 Differential diagnosis of the empty scrotum

Abnormalities of testicular descent/development
Primary cryptorchidism
Ectopic testis
Disorder of sexual differentiation (DSD)
46, XX DSD
46, XY DSD
Ovotesticular DSD
Sex chromosome DSD
46, XX testicular DSD
Other abnormalities of the testis
Perinatal torsion
Retractile testis
Ascending testis
Testicular atrophy

female with congenital adrenal hyperplasia (CAH). One type of CAH includes a salt wasting form which can be fatal if the diagnosis is missed. This variety of the disease must be ruled out prior to discharge from the hospital for these infants. Evaluation should consist of electrolytes, karyotype, 17-OH progesterone, testosterone, LH, FSH, pelvic ultrasound, and possibly a genitogram.

4. CAH is the most common cause of ambiguous genitalia in neonates and can result in virilization of the female and in aldosterone deficiency. It results from a deficient enzyme in the glucocorticoid synthesis pathway and is inherited in an autosomal recessive fashion. The most common of these disorders is 21-hydroxylase deficiency, found in 95 % of the cases of CAH. Of these, three-fourth are salt wasters (i.e., have aldosterone deficiency). Symptoms can include weight loss, dehydration, and severe emesis. Measurement of 17-OH progesterone helps to establish the diagnosis of CAH.
5. Adrenal crisis can occur in patients with CAH within the first 10–21 days of life. Death can occur from hyperkalemia, dehydration, and shock; immediate stabilization, diagnosis, and treatment are paramount.
6. The child with ambiguous genitalia should undergo a multidisciplinary evaluation involving urology, endocrinology, and genetics. Psychological support may also be useful as the family works through the diagnosis. Further laboratory and radiologic evaluation may be necessary. Decisions regarding the gender assignment and timing and type of genital reconstruction are complicated and can be controversial. It is important that the medical specialists and the family function as one team during this process.
7. Most UDTs are palpable and unilateral. Approximately three-fourth are able to be palpated; unilateral disease is found in 60–70 %. Testicles that are found to be descended on repeat examination are in need of continued observation as there is a potential for ascension of the testicle as the child grows; these specific follow-up exams can generally be conducted by the primary care physician. Nonpalpable testes are less likely to descend to the scrotum on repeat exam and could thus be referred upon diagnosis.

8. Spontaneous descent of a testicle after birth has been described with varying rates. By 3 months of age, the incidence of UDTs has generally been found to be 1–2 %. Spontaneous descent is more likely in less severe disease (i.e., a high scrotal testis is more likely to descend than an extrascrotal testis). History of prematurity is also related to a greater likelihood of spontaneous descent.
9. Surgical intervention for the diagnosis of UDT is unlikely to be undertaken prior to 3 months of age. It is therefore reasonable, given the potential for spontaneous descent, to reexamine the patient with a palpable, but undescended, testicle at that point in time to determine whether referral is necessary. The potential for spontaneous descent declines after 3 months of age.
10. For the patient with a persistent and/or nonpalpable, undescended testicle, referral to the urologist is warranted. There are several indications for correcting cryptorchidism. These include (1) optimization of testicular function and fertility potential, (2) enhanced ability to monitor for development of testicular malignancy as well as potentially decreasing the overall risk of testicular cancer, (3) correction of commonly associated hernia/hernias, (4) psychological and cosmetic benefit of having a "normal" appearing scrotum, and (5) reduction in the risk of testicular torsion. Paternity rates have been demonstrated to be 65 % for those with a history of bilateral UDTs, 90 % for unilateral UDTs, and 93 % in normal controls. The relative risk of malignancy has been shown to be 2.5–8 in those with a UDT; the risk in those who have undergone orchiopexy before puberty is two to three-fold higher than normal. Given these risks, an age-appropriate discussion of the importance of testicular self-examination should be conducted with the patient and his family.

 In the past, surgical, medical, and even observational approaches have been described for UDTs. Currently, most would prefer and recommend the surgical approach to correcting the disease process. Inguinal, scrotal, and laparoscopic approaches are commonly utilized for the UDT. The choice of approach is in part dependent on the palpability of the testicle, the examination of the contralateral testicle, age of the patient, and surgeon preference. Medical therapy has been used in a variety of settings and is based on the theory that testicular descent is promoted by androgens. Studies have involved both LHRH and hCG, but overall the efficacy of these hormonal therapies has been questioned. Indeed, consensus statements have gone so far as to recommend against the routine use of these medical interventions. Data regarding long-term observational approaches are less robust and are generally not recommended.

Conclusion

The empty scrotum can be indicative of a range of disorders, from primary cryptorchidism to DSD. For the child to receive proper care, it is critical that the primary care physician/pediatrician recognizes these disorders. Urologists play a large role in the overall care of these patients and decisions regarding surgical intervention. Following surgical treatment, patients will need counseling regarding testicular self-examination for malignancy, particularly as they enter puberty and progress through adulthood.

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Chapter 6
Priapism

Giulio Garaffa and David J. Ralph

Abstract Priapism is defined as a persistent erection that is unrelated to sexual stimulation or continues for more than 4 h beyond sexual stimulation and orgasm. Priapism can then be subdivided into the three different categories: (1) low flow (ischemic), (2) stuttering, and (3) high flow (nonischemic).

Keywords Priapism • Low flow • High flow • Stuttering • Erectile dysfunction • Penile prosthesis

Introduction

Priapism is defined as a persistent erection that is unrelated to sexual stimulation or continues for more than 4 h beyond sexual stimulation and orgasm.

Priapism can then be subdivided into the three different categories: (1) low flow (ischemic), (2) stuttering, and (3) high flow (nonischemic). Comparative characteristics of the three different types of priapism are reported in Table 6.1.

1. *Low flow priapism*, which accounts for more than 95 % of all priapic episodes, is a compartment syndrome at the level of the corpora cavernosa and is characterized by a persistent painful erection with little or absent inflow through the cavernosal arteries, as demonstrated by the color Doppler ultrasound scan (ECDUSS).

 In the majority of cases, priapism is idiopathic with blood dyscrasias, recreational drugs and alcohol abuse, malignancy, neurological diseases, intracavernosal

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Table 6.1 Comparative characteristics of the different types of priapism

	Low flow	Stuttering	High flow
History of trauma	No	No	Yes
Erection	Full	Full	Partial tumescence
Pain	Yes	Yes	No
Blood dyscrasias/drug abuse	Yes	Yes	No
Duration	>4 h	<3 h	Any
Spontaneous resolution	No	Yes	No
Peak systolic velocity (ECDUSS)	Low or absent	Low or absent	>25 cm/s
Cavernosal blood gas analysis			
PH	Reduced	Reduced	Normal
O_2	Reduced	Reduced	Normal
CO_2	Increased	Increased	Normal
Glucose	Reduced	Reduced	Normal

injection of vasoactive drugs, and phosphodiesterase type 5 inhibitors (PDE5i) accounting for the remaining 30–40 % of episodes.

As the arterial inflow is reduced, there are time-dependent changes in the corporal metabolic milieu that lead to progressive hypoxia, hypercarbia, acidosis, and glucopenia. This induces a progressive damage to the smooth corporeal muscle that becomes progressively irreversible as ischemia time continues. Although it is still matter of debate the precise time when this process becomes irreversible, intervention after 48–72 h may help to relieve the pain and settle the erection but will not be able to reverse the necrosis of the smooth muscle. The necrotic smooth muscle will then be progressively substituted by scar tissue with consequent penile shortening and onset of refractory erectile dysfunction. Therefore, low flow priapism is an emergency and requires immediate treatment as any delay in the management can translate into an increased risk of onset of severe erectile dysfunction and penile shortening.

2. *Stuttering priapism* is characterized by a pattern of recurrence and is particularly common in men with sickle cell disease; typically patients are awakened by erections that persist for less than 3 h and progressively become painful due to the progressive onset of ischemia. It occurs repeatedly with intervening periods of detumescence, and if the episodes are not treated, it may evolve into a classic ischemic priapism and eventually lead to irreversible corporal fibrosis with permanent erectile dysfunction. Patients with stuttering priapism usually suffer embarrassment, sleep deprivation, and performance anxiety.
3. *High flow priapism* instead is a persistent erection caused by unabated cavernosal arterial inflow and typically is characterized by a non-painful semi-erect penis. It is consequence of the traumatic disruption of the anatomy of the cavernosal artery with formation of an arteriosinusoidal fistula.

Although the most common cause is blunt trauma to the corpora, high flow priapism has been also been described following direct vision optical urethrotomy, needle injury

Table 6.2 Management of the different types of priapism

Type of priapism	First-line treatment options	Second-line treatment options
Low flow	Aspiration	Immediate implantation of a penile prosthesis if medical treatment fails
	Instillation of phenylephrine (200 mcg repeated to a maximum of 1,500 mcg)	
	Shunt surgery (obsolete)	
Stuttering	Hormonal manipulation (GnRH agonists, diethylstilbestrol, antiandrogens, ketoconazole)	Penile prosthesis implantation
	α_1 (pseudoephedrine and etilefrine)- and β_2-agonists (terbutaline) to increase smooth muscle tone	
	PDE5i	
	If >4 h treat as low flow	
High flow	Compression	Superselective embolization of cavernosal artery with desorbable material
	Ice packs	

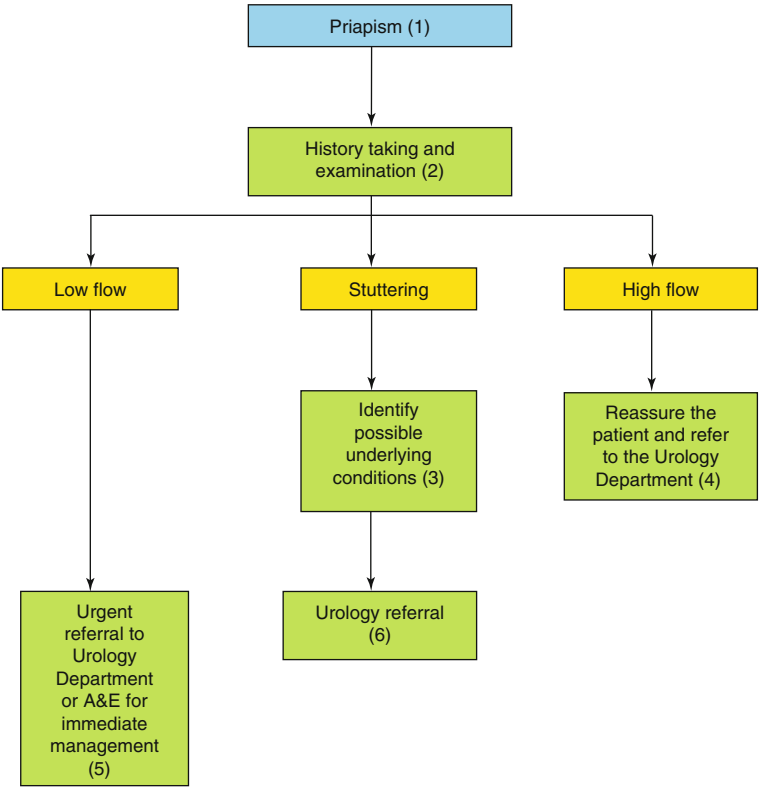
during hydraulic artificial erection, and penile revascularization. Since there is continuous arterial inflow, the cavernosal tissue does not become ischemic and cavernous blood gas analysis does not show hypoxia, hypercarbia, glucopenia, and acidosis. Emergent intervention is not necessary in high flow priapism as ischemic damage does not occur, patients do not report penile pain, and normal erectile function is maintained.

Although the management of priapism is a province of the urologist (Table 6.2), the aim of this chapter is to provide the GP with a practical algorithm that allows the making of a differential diagnosis between low flow priapism, which requires immediate intervention, and intermittent and high flow priapism, which can be managed more electively.

Basic Investigation and Management of Priapism

Comments About Flowchart 6.1

1. Any patient presenting with prolonged erection (lasting more than 4 h) unrelated to sexual stimulation fulfills the definition of priapism.
2. History taking and examination are the mainstay of the diagnosis of priapism at the GP practice. Comparative characteristics to distinguish between the three types of priapism based on patient's history and examination are reported in Table 6.1. In the case of suspected low flow priapism, the patient needs to be referred immediately to the local Urology Department, as further investigations such as cavernosal blood gas analysis and ECDUSS would just unnecessarily delay



Flowchart 6.1 Priapism

treatment. Low flow priapism should be suspected in presence of prolonged erection, pain, and full penile rigidity. A medical history significant for blood dyscrasias, recreational drug abuse, neurological conditions, intracavernosal injection of vasoactive drugs, and use of PDE5i confirms the suspicion. Patients with history of stuttering priapism usually do not present to the GP practice with the priapic episode, as the erections are usually nocturnal and last less than 3 h. High flow priapism instead can be easily recognized from a history of blunt genital trauma or urethral instrumentation and is characterized by a non-tender penis with a partial erection.

3. In case of stuttering priapism, the vast majority of patients have already been diagnosed with sickle cell anemia. In idiopathic cases, the presence of blood dyscrasias should be ruled out prior to referring to the Urology Department.
4. Patients with high flow priapism do not need to be managed urgently as there is no ischemia in the corpora cavernosa. Initial management is compression and application of ice with the aim of inducing vasospasm of the cavernosal artery with clot formation and obliteration of the fistula. If conservative management does not suffice, superselective embolization of the cavernosal artery should be attempted

under radiological guidance. It is paramount to use absorbable embolizing materials such as clot or foam instead of unabsorbable coils. In fact, unabsorbable materials obstruct the arterial flow only for a short period of time to allow for the fistula to heal, and then they dissolve allowing a complete recover of the cavernosal artery flow.

5. The clinical diagnosis of low flow priapism can be confirmed with ECDUSS scan, which shows minimum or absent arterial inflow, and with corporeal blood gas analysis, which demonstrates hypoxia, hypercarbia, glucopenia, and acidosis. It is paramount not to perform the ECDUSS after the aspiration of the corpora, as the investigation may then falsely suggest a high flow pattern. MRI scan of the penis may play a role in the early detection of necrosis of the cavernosal smooth muscle, but data in the literature are contradictory. The initial conservative management of low flow priapism consists of aspiration of the corpora cavernosa and repeated instillations of α-mimetic agents such us phenylephrine (200 mcg repeated to a maximum of 1,500 mcg) in an attempt to constrict penile arteries and thus reduce arterial penile blood inflow. If this maneuver fails to induce detumescence, it is likely that irreversible ischemic changes in the corpora have already occurred and as a consequence the cavernosal smooth muscle is not able to contract as a response to phenylephrine stimulation. If smooth muscle necrosis has already occurred, any attempt to reoxygenate the corpora performing shunt surgery will prove futile, as this will not prevent the necrotic muscle from being progressively substituted by scar tissue with consequent penile shortening and onset of refractory erectile dysfunction. Ultimately, these patients will require implantation of a penile prosthesis, which will be associated with low satisfaction rate, due to the high complication rates and the severe penile shortening. Therefore, patients who have not responded to aspiration and instillation of phenylephrine and who are sexually active should be offered the immediate insertion of a penile prosthesis as this timely procedure resolves the priapic episode, allows the patient to maintain the rigidity necessary to achieve penetrative sexual intercourse, and prevents penile shortening.
6. Patients with stuttering priapism should be referred to the Urology Department for management. Treatment is not urgent, but patients must be warned that in case of erection lasting longer than 4 h, they must seek immediate attention and should be managed as for low flow priapism. Oral α-mimetic agents such as pseudoephedrine and etilefrine and low dose PDE5i have been successfully used in patients with sickle cell anemia as a first-line treatment as they increase the tone of the cavernosal smooth muscle and prevent its relaxation. Hormonal manipulation should be offered to patients when the first-line treatment fails and consists of the suppression of the circulating levels of testosterone, which is the hormone responsible of triggering the priapic episodes. Testosterone suppression can be achieved either by downregulating the pituitary gland with GnRH agonists, by reducing adrenal and testicular testosterone production with ketoconazole, or by blocking androgen receptors with antiandrogens. Patients who do not respond or do not tolerate medical treatment are offered surgical treatment. Ideally, surgical treatment should prevent unwanted erections, but not compromise the ones related to sexual stimulation. Therefore, the best solution is the

implantation of three-piece inflatable penile prosthesis, which allows both a flaccid and an erected state of the penis. Embolization or ligation of the cavernosal artery should be discouraged as they result in a complete, permanent loss of all erectile functions.

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Chapter 7
Swollen Penis

Giulio Garaffa and David J. Ralph

Abstract Genital lymphoedema and penile fracture represent the most common causes of swollen/painful penis. This chapter focuses on the diagnostic tools required for the diagnosis and on the treatment options of these two conditions.

Keywords Penile fracture • Erectile dysfunction • Lymphoedema • Elephantiasis

Introduction

Genital lymphoedema and penile fracture are the two most common causes of penile swelling.

Penile fracture (Fig. 7.1) can be defined as the rupture of the tunica albuginea of the corpora cavernosa and occurs in the erect state where elongation and thinning of the tunica albuginea occurs. The site of the tear is usually ventrolateral and transverse in the proximal half of the shaft where the tunica is weakest, being a single layer structure in this area; however, longitudinal distal fractures have been described in up to 30 % of cases. An associated urethral injury can be found in up to 33 % of cases. Penile fracture is usually consequence of the excessive ventral angulation that occurs when the penis hits the female pelvis during enthusiastic sex. However, cases of penile fracture secondary to vigorous masturbation or kneading of the penis to achieve detumescence have been described, especially in the series from the Middle East and North Africa.

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Fig. 7.1 Haematoma caused by a penile fracture. The subcutaneous haematoma extending to scrotum and perineum (butterfly sign) indicates that the penile fracture is associated with breach of Buck's fascia

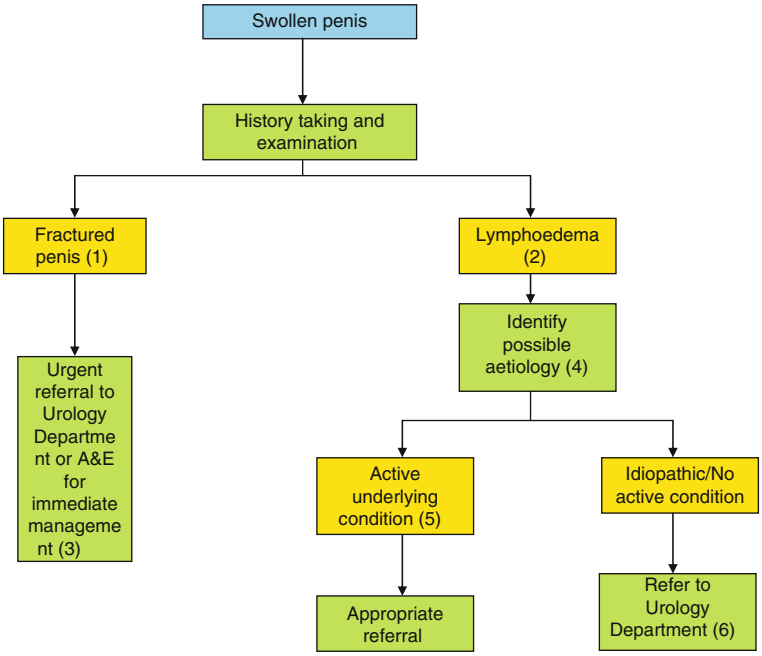


Fig. 7.2 Genital lymphoedema localised to the penis. Due to the recent onset of the condition, the penile skin looks still healthy

Genital lymphoedema (Fig. 7.2) may occur in isolation with either the scrotum, penis or both being involved, or it may be combined with generalised lower limb oedema and is thus the consequence of impaired lymphatic drainage leading to abnormal retention of lymphatic fluid. All conditions that may affect the lymphatic drainage of the penis and scrotum may lead to the formation of lymphoedema with surgical interventions, trauma, radiotherapy, malignant infiltration and granulomatous and venereal diseases being the most common causes.

The progressive genital swelling can be extremely debilitating compromising both urinary and sexual function, and recurrent episodes of cellulitis lead to the deposition of scar tissue that renders the skin so thickened that the condition is known as elephantiasis.

This chapter will provide a practical algorithm that allows making a differential diagnosis between penile fracture and penile lymphoedema and give an insight regarding the management of the two conditions.



Flowchart 7.1 Swollen penis

Basic Investigation and Management of Swollen Penis

Comments About Flowchart 7.1

1. The diagnosis of penile fracture is largely clinical. The classical features of penile fracture are a snapping sound followed by immediate detumescence, swelling and shaft contusion. If Buck's fascia has been breached, the haematoma will track to the base of the shaft or spread to the perineum, scrotum (butterfly sign) and lower abdominal wall (Fig. 7.1). Isolated urethral rupture and rupture of deep or superficial dorsal vein or of the deep dorsal artery of the penis may present with a clinical scenario similar to the one of the classical penile fracture and therefore must be excluded with accurate history taking, examination and imaging. Blood per urethra, difficulty to pass urine or inability to introduce a catheter are obvious signs of urethral fracture but they may not be apparent even when the urethra has been completely divided.
2. The diagnosis of genital lymphoedema is largely based on examination that shows a localised or diffuse swelling of the dartos fascia (Fig. 7.2). It can be easily distinguished from penile fracture as there is no previous history of trauma, no haematoma is visible and usually there is no pain unless cellulitis and skin maceration are present. Moreover, the onset of penile lymphoedema tends to be subtle and slow in contrast with the acute one that characterises penile fracture.

Table 7.1 Differential diagnosis between penile fracture and lymphoedema

Characteristics	Lymphoedema	Penile fracture
Pain	No (unless cellulitis or ulceration is present)	Yes
History of recent trauma	No	Yes
Haematoma	No	Yes (if Buck's fascia is breached)
Bleeding from meatus	No	If concomitant urethral tear
Onset of swelling	Slow and progressive	Acute
Underlying condition	Common	No

A summary of differential clinical features between penile fracture and penile lymphoedema is reported in Table 7.1.

3. If a penile fracture is suspected, the patient needs to be urgently referred to the urology department. MRI and USS of the penis may be useful to identify the site of the albugineal tear and to exclude the presence of an associated urethral injury. However, with regard to the detection of associated urethral injury, the sensitivity of both investigations is not extremely high. Conservative management can be offered only if a urethral tear can be excluded. Since conservative management leads to significant scar formation and corporal fibrosis with consequent penile shortening and bending, pseudoaneurysm formation and erectile dysfunction, early surgical repair represents the mainstay of treatment. Surgery involves the exposure and repair of the albugineal tear and of any associated urethral rupture and the evacuation of haematomas and yields excellent cosmetic and functional results with less than 5 and 1 % of patients developing, respectively, penile curvature and erectile dysfunction.
4. In genital lymphoedema, the priority is to identify and manage the underlying condition, particularly if infection, systemic disease and underlying malignancy are suspected.
5. If an underlying condition is identified, the patients should be appropriately referred. Most early-stage lymphoedema settles with conservative measures once the underlying condition has been successfully treated.
6. The initial management of genital lymphoedema is conservative with compression and elevation of the genitalia and administration of broad-spectrum antibiotics to prevent recurrent bouts of cellulitis, which would eventually destroy the elasticity of the skin. If the underlying condition is adequately treated, most early-stage lymphoedemas settle with just conservative measures. Large or long-standing lymphoedemas do not respond to medical treatment as the repeated bouts of cellulitis have resulted in the destruction of the elastic fibres that are substituted by scar tissue. These patients require referral to a urology department specialising in reconstruction as the only management consists in the complete excision of the lymphoedematous tissue followed by repair with local flaps and skin grafts.

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Chapter 8
Penile Ulcer and Balanitis

Hussain M. Alnajjar, Majid Shabbir, and Nicholas A. Watkin

Abstract Patients may present with a variety of different dermatological conditions affecting the penis, ranging from rashes and red patches to ulcers or problems with the foreskin. The majority of penile dermatoses are benign and harmless lesions, which can be managed with simple conservative measures. However, a small number of patients may present with premalignant or even early malignant lesions of the penis. Detecting the "wolf in sheep's clothing" can be difficult but is essential to allow early referral and prompt curative treatment.

The aim of this chapter is to provide a stepwise, practical guide on how to identify and manage penile lesions and balanitis in the primary care setting. This will encompass how and when to perform basic investigations, and how to manage these patients appropriately without compromising their care or clinical outcome.

Keywords Balanitis xerotica obliterans • Lichen sclerosis • Carcinoma in situ (CIS) • Penile intraepithelial neoplasia (PIN) • Penile ulcer • Benign penile lesions • Penile cancer

Introduction

Patients may present with a variety of different dermatological conditions affecting the penis, ranging from rashes and red patches to ulcers or problems with the foreskin. The majority of penile dermatoses are benign and harmless lesions, which can

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be managed with simple conservative measures. However, a small number of patients may present with premalignant or even early malignant lesions of the penis. Detecting the "wolf in sheep's clothing" can be difficult but is essential to allow early referral and prompt curative treatment.

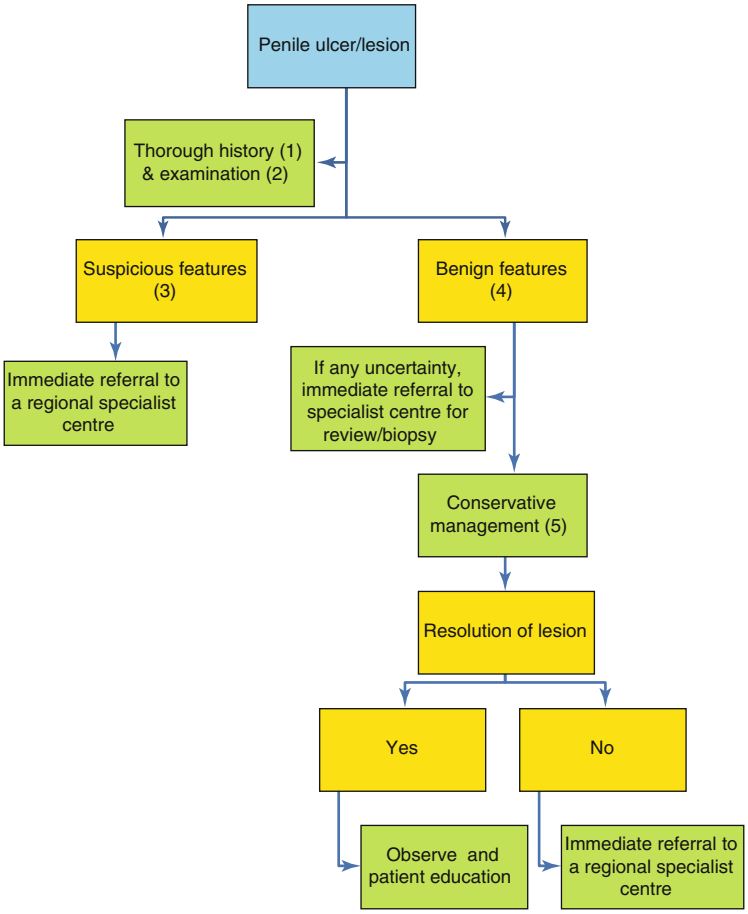
The aim of this chapter is to provide a stepwise, practical guide on how to identify and manage penile lesions and balanitis in the primary care setting. This will encompass how and when to perform basic investigations, and how to manage these patients appropriately without compromising their care or clinical outcome.

Basic Investigation and Management of Penile Ulcer

Comments About Flowchart 8.1

1. *History*: Important aspects in the history include details on the duration and nature of the lesion. Painful ulcers are more typical of herpes, aphthous ulceration, and fixed drug eruption. Malignant lesions are generally painless initially. Any lesion with a history of rapid change or bleeding should also raise suspicion of malignancy. The history should focus on known risk factors associated with penile cancer, including a history and timing of any circumcision, a history of phimosis, poor hygiene, smoking, psoralen ultraviolet A (PUVA) therapy for psoriasis, immunosuppression/human immunodeficiency virus (HIV) infection, and human papillomavirus (HPV) infection (present in ~50 % of cases of penile cancer). Penile cancer is almost unheard-of in patients circumcised at birth but is more common in patients who are circumcised as an adult due to phimosis. A detailed sexual history including age of first sexual contact, number of sexual partners, and history of sexually transmitted diseases should also be sought. A history of extragenital dermatoses should be excluded (psoriasis). A focus on drug history should exclude the possibility of a drug reaction; nicorandil has been associated with penile ulceration.
2. *Examination*: The examination should focus on every aspect of the penis, including the glans, the meatus, the foreskin, and the penile shaft. Inspection should also include the scrotum, perineum, and inguinal regions. The penis should be assessed for the presence/absence and condition of the foreskin. Evidence of phimosis and level of hygiene should also be assessed. The presence, pattern, and size of any lesions, red areas and areas of pigmentation, lichenoid changes, or ulceration should be recorded.
3. *Suspicious Features*: Moist red ulcer/lesion (raised, velvety), an asymmetrical lesion, history of rapid growth, history of bleeding, presence of a hard irregular lump, or exophytic growth should raise suspicion of a malignancy. Specific features of important premalignant lesion include:

 (a) Erythroplasia of Queyrat (EQ): squamous cell carcinoma in situ of the glans penis. It is usually associated with HPV 16. Up to 30 % of EQ progress to squamous cell carcinoma of the penis. Lesions are usually sharply defined



Flowchart 8.1 Penile ulcer

plaques, which have a smooth, velvety, bright red appearance. They are usually painless, but can have areas of erosion. The vast majority occurs in uncircumcised men with phimotic foreskins.

(b) Bowen's disease (BD): carcinoma in situ lesions on the keratinized shaft of the penis or prepuce. Lesions are usually solitary, well-defined, scaly, dull-red plaques. Some may also be heavily pigmented, resembling melanoma. Occasionally they may have associated leukoplakic, nodular, or ulcerated changes. Malignant transformation has been reported in 5 % of cases.

(c) Bowenoid papulosis (BP): occurs primarily in young sexually active men. Lesions are usually seen on the shaft, but can also occur on the glans and prepuce. They are usually multiple, red, velvety lesions but can have brown pigmentation. They often coalesce into larger plaques and are itchy. They carry a very small risk of malignant transformation (<1 %).

(d) Giant condyloma acuminatum (GCA): confluence of warty, exophytic growths, which are usually seen on the coronal sulcus and frenulum. Reported rates of malignant transformation are between 30 and 56 %.

4. *Benign Features/Lesions*:

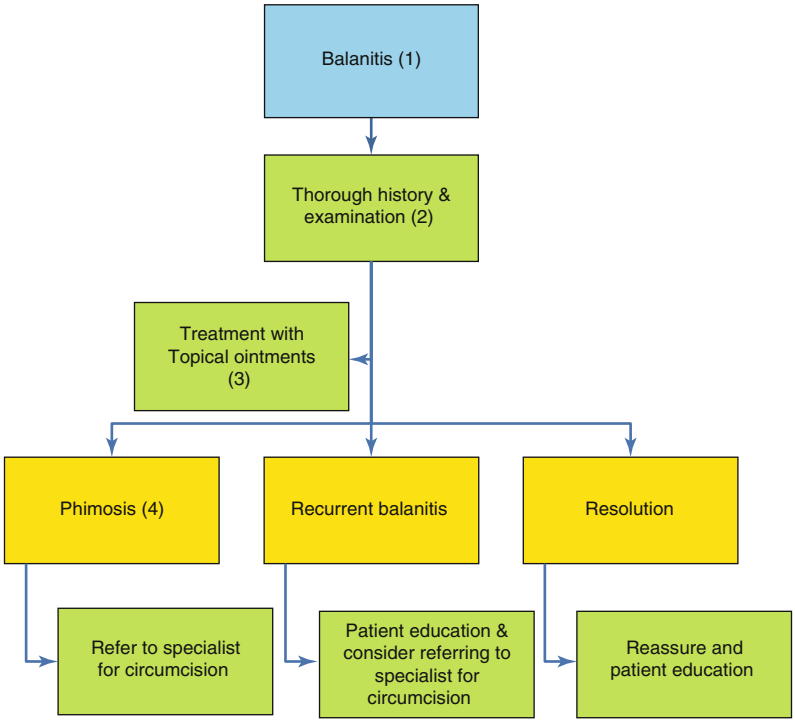
(a) *Pearly penile papules*: multiple, little white papules around the circumference of the corona of the glans and occur usually in postpubertal males. They are not infectious and require no treatment.
(b) *Zoon's balanitis*: see below in the section on balanitis.
(c) Aphthous ulcers and syphilitic chancres are painful, usually well-circumcised lesions, and have well-demarcated edge.
(d) *Lichen sclerosus* (*LS*): also known as *balanitis xerotica obliterans* (*BXO*); this is a common sclerosing condition of glans and prepuce. It occurs at all ages. Patients often have pale, atrophic/sclerotic plaques on the glans but can also present with red "zoonoid" inflammatory lesions. Most commonly, it presents as a nonretractile foreskin (phimosis). Phimosis invariably leads to retention of the normally desquamated epidermal cells and urinary products (smegma), which can result in balanitis or balanoposthitis (see below). The meatus and fossa navicularis may also be affected, causing obstructed and spraying voiding. The diagnosis is histological and usually made after circumcision. Although LS is often found in association with penile cancer, it remains unclear whether it is a true premalignant process. Development of penile cancer in patients with known LS is low (5 %), with a long latency (17 years).
(e) *Nonspecific balanoposthitis*: inflammatory condition of glans and foreskin. Can be caused by bacterial and candidal infections.
(f) *Psoriasis*: appears as thickened red papules or plaques with well-defined edges and often has a scaly surface. Genital lesions do not tend to occur in isolation.

5. *Conservative Management*: Includes treatment of the lesion with a short course (4 weeks) of topical steroid creams (e.g., 0.05 % clobetasol BD) and antifungals (e.g., 1 % clotrimazole TDS) if a fungal infection is suspected. Switching to a soap substitute is also recommended. Close observation of the lesion with regular follow-up, patient education, and advice on regular self-examination is essential. Patients should be encouraged to have a low threshold to report back if the lesion increases in size or does not respond to treatment. Referral to a regional specialist center should be made for any cases where there is a failure to respond to first line topical steroid therapy, or when the exact diagnosis is unclear.

Basic Investigation and Management of Balanitis

Comments About Flowchart 8.2

1. *Balanitis*: Is a common condition affecting 11 % of adult men seen in urology clinics and 3 % of children. It refers to inflammation of the glans penis. When the foreskin is involved, the term balanoposthitis is used instead.



Flowchart 8.2 Balanitis

2. *History and Examination*: A thorough history including the onset of the symptoms and associated features such as soreness, irritation, redness, and foul-smelling discharge is important for diagnosis. Poor personal hygiene plays an important role, combined with a tight foreskin (phimosis), which can lead to irritation by retained smegma. Smegma is a whitish curd-like substance, which forms under the foreskin if the glans under the prepuce is not cleaned regularly. This is the most common cause of balanitis. Infection with candida (thrush), bacterial infections, and sexually transmitted infections (STI) can also cause acute balanitis. It is important to carefully examine the penis to establish a diagnosis. Findings can range from a small patch of redness confined to part of the glans, to the whole glans becoming red, swollen, and painful.

 (a) *Zoon's balanitis* is an idiopathic condition, which occurs in middle-aged and elderly men who are not circumcised. It usually presents as a bright shiny red plaque on glans penis or inner prepuce, with a symmetrical "kissing contact" pattern. It can be treated by topical ointments, although circumcision is often required to ensure resolution. If the patient is asymptomatic, it can be left without any intervention. It can often be difficult to distinguish from EQ or zoonoid inflammation in LS, and if the diagnosis is in doubt, referral to a specialist center for incisional biopsy is recommended.

3. *Treatments*: Moderate potency topical steroids such as 0.05 % clobetasol propionate are applied thinly one to two times daily for up to 4 weeks for inflammatory balanitis. Antifungals such as 1 % clotrimazole (two to three times a day for 4 weeks) are usually used when a fungal infection is suspected. Two percent fusidic acid (three to four times daily for 4 weeks) should be prescribed if a staphylococcal infection is suspected. Antibiotics are used instead of steroids if an infective process is thought to be the route cause (a 1-week course of oral co-amoxiclav 375 mg TDS or clindamycin 300 mg QDS if penicillin allergic). Patients with suspected STI should be managed in conjunction with the local GU clinic.
4. *Phimosis*: Refers to a tight, nonretractile foreskin often found in association with balanitis. Topical steroids are not effective for established phimosis and often only temporarily stabilize the situation. The best treatment for phimosis is circumcision. Circumcision plays a pivotal role in the management of patients with penile dermatoses. It not only allows removal of the dysfunctional foreskin, with treatment of lesions confined to the prepuce, but it also eliminates the microenvironment under the foreskin, which is conducive to inflammation and persistence of HPV infection. It also facilitates surveillance and self-examination of the glans penis and forms an important part of managing penile dermatoses.

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Chapter 9
Gross (Visible) Hematuria

Paolo Gontero

Abstract Gross hematuria, even as a single episode, can be the presenting sign of a cancer of the urinary tract. At the same time, several benign diseases can present with hematuria although it is not always possible to prove a direct relationship between the two. As a result, the cause of hematuria will remain unknown in a significant proportion of cases even after an intense diagnostic workup. While most of the patients will eventually need a urological referral, the degree of urgency largely depends upon the risk of the patient having a malignancy. The aim of this chapter is to help the GP in the deciding which case of hematuria needs an urgent specialist referral and which can be managed in the first instance by the GP himself with a full diagnostic workup followed by a delayed referral. A 3-step diagnostic algorithm is proposed, starting from the evaluation of the severity of hematuria (step 1), moving on to the differential diagnosis among the most common etiologies of hematuria based on patient's history and examination (step 2). Finally a diagnostic flowchart tailored to patients belonging to different risk categories is proposed (step 3).

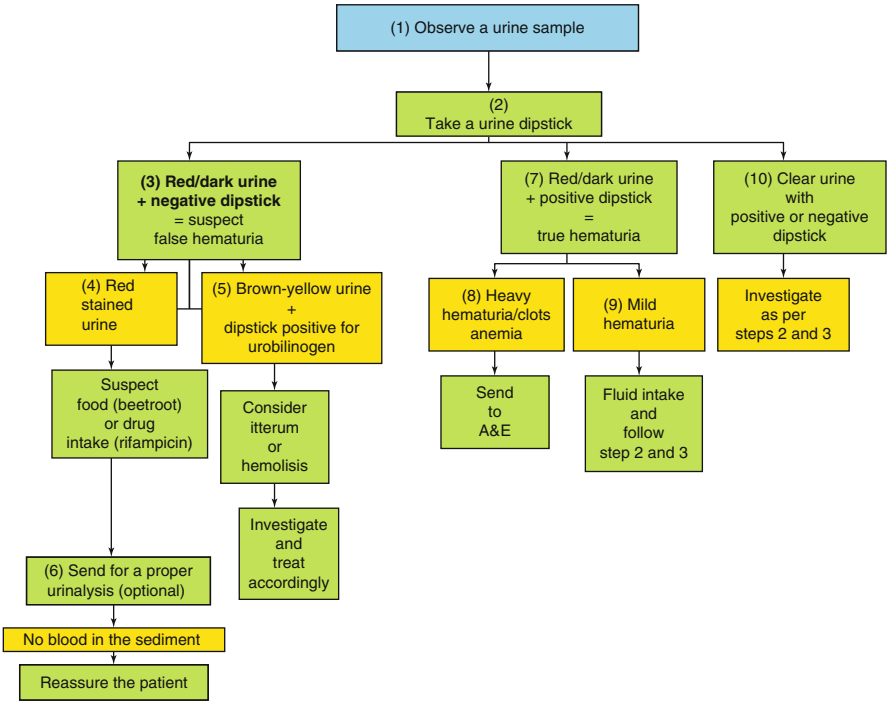
Keywords Hematuria • Macroscopic • Gross • Bladder cancer • Urothelial cancer • False hematuria

Introduction

Hematuria can be divided into *gross* (*visible*) *hematuria* and *microscopic* (*non-visible*) *hematuria*. In the first instance, the patient is aware of the symptom and may present in the office with bloodstained urine, or report a history of hematuria with clear

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Flowchart 9.1 First line decision making for gross hematuria

urine in the present time. In this chapter, a practical guide to approach gross hematuria will be provided as a 3-step decision-making algorithm. Microscopic hematuria will be addressed in Chap. 26.

Diagnostic and Treatment Steps

Step 1: Is It a True Hematuria? Does It Need Urgent Treatment?

Comments About Flowchart 9.1

1. When a patient presents to the clinic complaining of "red" urine, the first action should be to ask him to produce a *urine sample*. A macroscopic hematuria will be easily recognized although the rare occurrence of so-called "false" hematuria has to be taken into account.
2. A *urine dipstick* is a simple and cheap test that can be easily performed in the office to confirm the hematuria.

3. A *negative* urine dipstick is highly reliable (99 %) to exclude the presence of red blood cells or hemoglobin.
4. Some food (such as beetroot) or drugs (rifampicin) may produce a reddish stain of the urine. A detailed food and drug history is mandatory.
5. A dipstick positive for *urobilinogen* may suggest the presence of jaundice or hemolysis and should be investigated and treated accordingly.
6. It is recommended that a urine sample is sent for a urinalysis. Absence of red blood cells in the sediment will further support the presence of "false hematuria." Do not forget that red-dark colored urine in the presence of a dipstick and sediment negative for blood may rarely be due to the presence of myoglobin (rhabdomyolysis) or porphyrins in the urine.
7. A positive dipstick will confirm the presence of true hematuria.
8. Heavy hematuria, particularly if associated with clots and/or signs of severe anemia due to long-lasting hematuria, should prompt a referral to A&E as the patient will benefit from immediate investigations and actions (blood checks, catheterization and bladder washouts or irrigation with saline solutions, etc.).
9. Mild hematuria in absence of signs of severe anemia can be managed conservatively (high fluid intake, antibiotic if a urinary tract infection is suspected, etc.). Investigations (see steps 2 and 3) can be performed in an outpatient setting.
10. It is mandatory that any patient giving a history of possible hematuria follows steps 2 and 3, even if in the office his urine is clear and no blood can be traced with the dipstick.

Step 2: Formulate a Diagnostic Hypothesis

Several clinical situations may sustain a hematuria. While the number one priority of the physician is to rule out any underlying tumor sustaining the hematuria, the etiology of the majority of hematuria cases will eventually remain unknown (50 %) or reside in a benign disease (30 %).

A detailed medical history including the mode of presentation of the hematuria and a thorough examination of the patient are essential prerequisites for a diagnostic hypothesis. Below, some practical tables are provided for possible etiologies of hematuria based on clinical signs and symptoms. The tables list a number of possible diseases that may be suspected if the hematuria is accompanied by other symptoms (the so-called symptomatic hematuria) (Table 9.1) or if it presents without symptoms (asymptomatic hematuria) (Table 9.2) or if it occurs in children (Table 9.3).

Since there are no specific presentations of the hematuria to exclude with certainty a neoplastic condition, a genitourinary cancer (*found in 1 out of 5 hematuria cases*) *should always be suspected.*

Table 9.1 Diseases more often presenting with a symptomatic hematuria

Organ	Disease	Patient's history	Symptoms	Signs
Kidney	Post-streptococcal glomerulonephritis	Recent respiratory infection, age < 40	Edemas, hypertension	Oliguria
	Polycystic kidney	Family history	Flank pain	Chronic renal failure, palpable kidney mass
	Acute pyelonephritis	UTIs	High fever, flank pain, dysuria	Cloudy urine, painful kidney on examination
	Kidney trauma	Trauma	Flank pain	Flank hematoma
Urinary tract	Stones (pelvis, ureter, bladder)	History of urinary stones	Renal colic, dysuria	Painful kidney on examination
	Cystitis	UTIs, radiotherapy	Dysuria	Cloudy urines

Table 9.2 Diseases more often presenting with a non-symptomatic hematuria

Disease	Patient's history	Signs
Urothelial carcinoma (bladder, ureter, and pelvis) (20 %)	Smoking history, dye exposure, age > 50	Painless gross hematuria, clots, CRF, and suprapubic mass only in advanced diseases
BPH	Lower urinary tract symptoms	Large feeling prostate on PR
Kidney cancer (1 %)	–	Palpable kidney mass
Prostate cancer (0.6 %)	–	Hard feeling prostate on PR, high PSA
Clotting disease	Anticoagulation therapies, chemotherapy	Petechiae
Exercise-induced hematuria	Young age, associated with exercise	Generally light and rapidly self-resolving hematuria
Berger's glomerulonephritis	Occasional gross hematuria with persistent non-visible hematuria	None
Uric acid urinary crystals	History of renal colic	Can occasionally present with asymptomatic hematuria

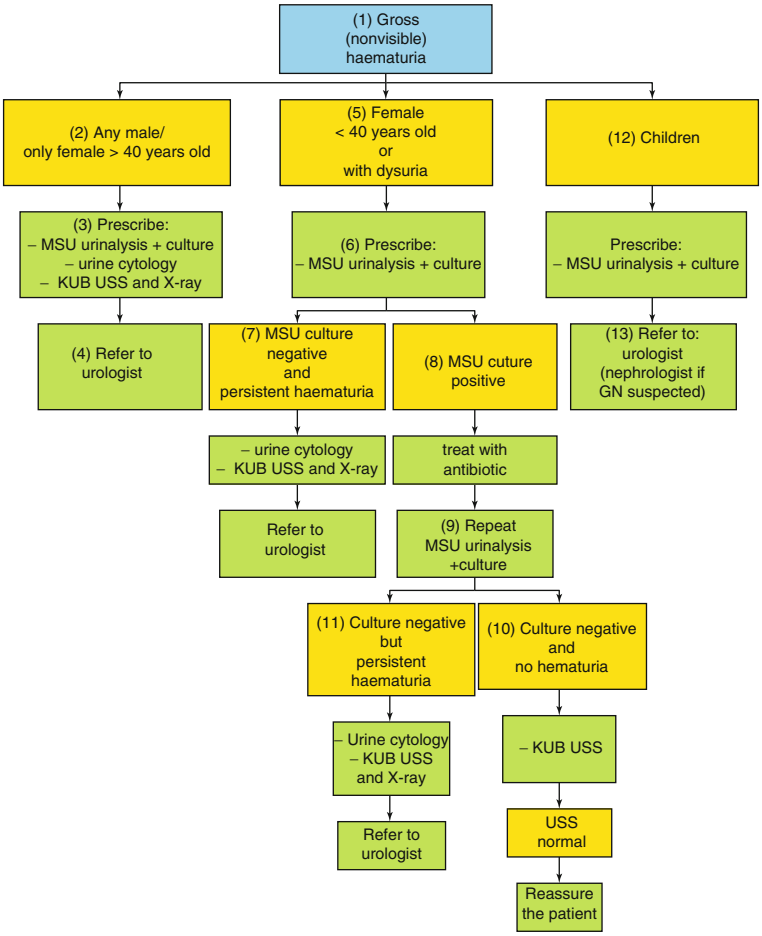
Table 9.3 Diseases more often causing hematuria in children

Disease	Patient's history	Symptoms	Signs
Acute glomerulonephritis	A respiratory infection in the preceding 2–3 weeks	Painless hematuria, coca-cola-like urines	Lower-extremity edemas, hypertension
UTIs	Female, vesicoureteral reflux	Abdominal pain, vomiting	Genital abnormalities
Idiopathic	Benign familial hematuria	Painless hematuria	None
Wilms tumor	–	Painless hematuria	Abdominal mass
Sickle cell anemia	Family history, African	None or pain at lower extremities	Anemia, fever, jaundice

Step 3: Decision Making

Comments About Flowchart 9.2

1. A gross hematuria, even at its first presentation, at any age, with or without accompanying symptoms, should always be investigated. Not all patients should be referred straightaway to the urologist; rather, initial investigation should be initiated by the GP in order to better select patients eventually needing specialist referral (urologist or nephrologist).
2. In any adult male presenting with gross hematuria, with or without other presenting symptoms, a cancer needs to be ruled out. Urothelial cancers can occasionally be found in male adolescents. While a urinary tract infection (UTI) is far less common in a male (as compared to a woman), cystitis-like symptoms can be associated with a bladder cancer. In females, urothelial cancers are far less common and a significant proportion of hematuria cases are due to UTIs. Since a hematuria of



Flowchart 9.2 Gross hematuria: how to investigate and refer to specialist care

neoplastic origin is extremely rare below the age of 40, it is advisable to start a thorough diagnostic workup in females above the age of 40.

3. A midstream specimen of urine (MSU) urinalysis plus culture, urine cytology, a plain X-ray of Kidney, Ureter and Bladder (KUB), and a KUB ultrasound (USS) are to be considered as first-line investigations for gross hematuria.
 - An MSU urinalysis with culture will help to rule out a UTI, highly suspected for the significant presence of nitrates, leukocytes, and bacterial growth.
 - A urine cytology should be preferably undertaken on the first morning urine on three samples from 3 consecutive days. Any suspicion raised by the urine cytology on the presence of atypical or neoplastic cells should be taken with great care and referred to a urologist. It should be remembered that urine cytology has a low sensitivity particularly for low-grade urothelial cancers and thus a normal test alone cannot be taken as a tool for reassurance (see also Chap. 27 for more details).

- A KUB USS has an excellent sensitivity to rule out a kidney tumor and to detect hydronephrosis, a sign potentially suggestive of a ureteric stone or of bladder and/or ureteric tumor. Sensitivity of the USS to detect a bladder tumor may be suboptimal for flat tumors and when the bladder is incompletely filled up.

4. Irrespective of the results of the above investigations, the patient should be referred to a urologist who will almost certainly carry out a cystoscopy and eventually further imaging tests (intravenous pyelogram or contrast CT).
5. Large series do not report urinary tract tumors in females below the age of 40 presenting with hematuria, the most likely cause being a UTI. A straight full hematuria workup for young females presenting with gross hematuria associated with cystitis-like symptoms is not necessary.
6. An MSU urinalysis with culture should represent the first-line investigation.
7. If a UTI cannot be demonstrated and hematuria (gross or microscopic) persists, the patient needs further investigations with a urine cytology, KUB, and USS. A urological referral will then follow.
8. If a UTI is demonstrated, specific antibiotic treatment will be administered.
9. An MSU urinalysis with culture needs to be repeated after 7–10 days from the end of the antibiotic course.
10. In case of a normal urinalysis with no further episodes of visible or non-visible hematuria, a KUB USS is advisable. If this comes back normal, no further action is needed and the patient can be reassured.
11. On the contrary, persistence of visible or non-visible hematuria requires further investigations (urine cytology, KUB X-ray and USS) and a urological referral.
12. In children, there is a tendency to investigate a gross hematuria in the same way as in the adult although urinary tract tumors are rare. The most frequent diseases usually arise from the renal parenchyma (Table 9.3). In a GP office, it is essential to rule out an underlying UTI, possibly a consequence of a vesicoureteral reflux. An MSU urinalysis with culture represents the first investigation.
13. In general, a young patient should be referred to the urologist (particularly in case of a proven UTI). A nephrological referral is preferable when clinical signs and urinalysis (proteinuria) are suggestive of a glomerulonephritis.

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Chapter 10
Urethral Bleeding

Paolo Gontero

Abstract Urethral bleeding is a relatively common reported event. Different etiologies characterize this symptom in males and females. In the male patient, urethral bleeding may suggest a urethral injury requiring urgent hospital referral. Other common causes of male urethral bleeding are linked to sexually transmitted diseases such as urethritis and condylomata of the urethral meatus. In a significant proportion of patients, the etiology of urethral bleeding will remain unknown, yet a urological referral is advisable to rule out the rare possibility of urethral neoplasms. In the female patient, it is usually more difficult to ascertain the urethral origin of bleeding because of possible confusion with an underlying gynecological (vulvovaginal or uterine) disease. Urethral examination usually helps to rule out benign conditions such as caruncles and diverticula as well as the rare occurrence of urethral neoplasms. In both sexes, the presence of urinary incontinence makes the differential diagnosis with hematuria difficult; hence, patients should be investigated accordingly. Unusual sexual practices that involve transurethral insertion of traumatic foreign bodies should always be kept in mind when considering urethral bleeding. A practical algorithm is provided to help the general practitioner in making decisions about female and male urethral bleeding.

Keywords Urethral bleeding • Urethral injury • Caruncle • Urethral condyloma • Urethral cancer

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Introduction

Urethral bleeding is defined as the occurrence of bleeding from the urethra separate from micturition. Patients should be asked to describe the circumstances when they noticed urethral bleeding in order to make sure they are not describing an episode of hematuria.

In a male patient, blood stained underwear in the area that is in contact with the penis is highly suggestive of urethral bleeding, after lesions in the genital skin or the gland have been excluded. Sometimes the patient has noticed one or more drops of blood pouring out of the urethral meatus not during episode of micturition. Spontaneous bleeding from the urethra implies that the site of origin of bleeding is distal to the striated sphincter, i.e., comprised in the bulbar, penile, or glandular urethra.

In the female, it is usually difficult, based only on the history of the patient, to discriminate between bleeding of uterine, vaginal, or vulvar origin (the far more common causes of bleeding) and urethral bleeding. A careful gynecological examination will help in the differential diagnosis.

For both sexes, when urine incontinence coexists, it becomes difficult to rule out bleeding from the urinary tract; hence, the patient should be investigated for hematuria.

Hints to Find a Cause for Urethral Bleeding

Table 10.1 lists the most common causes of urethral bleeding along with particular characteristics relating to the patient's history and the examination. It should be noted that, in spite of all the diagnostic investigations, in the majority of cases, the precise etiology of urethral bleeding will remain unknown.

The most common situation is minor trauma of the bulbar-penile urethra, usually occurring after the urethra is hit by a kick at the level of the penis or perineum. If the patient is able to void his bladder without significant pain and the urethral bleeding rapidly self-resolves, conservative management can be safely adopted. Any more complex situation should be referred to the A&E.

The management of complex urethral injuries is usually conservative, leaving a transurethral or suprapubic catheter in place. Complete urethral lacerations, particularly when associated with severe bleeding, may be treated with immediate surgical realignment of urethral stumps. Most urethral injuries will heal with a urethral stricture causing obstructive urinary symptoms. This complication needs to be promptly recognized, and the patient should be sent to the urologist for treatment.

Management of Urethral Bleeding in the GP's Office

Comments About Flowchart 10.1

1. A male patient describing urethral bleeding should be asked about the circumstances in which the symptom occurred (urethral injury, masturbation practices) and whether other symptoms are associated (chiefly urinary symptoms such as

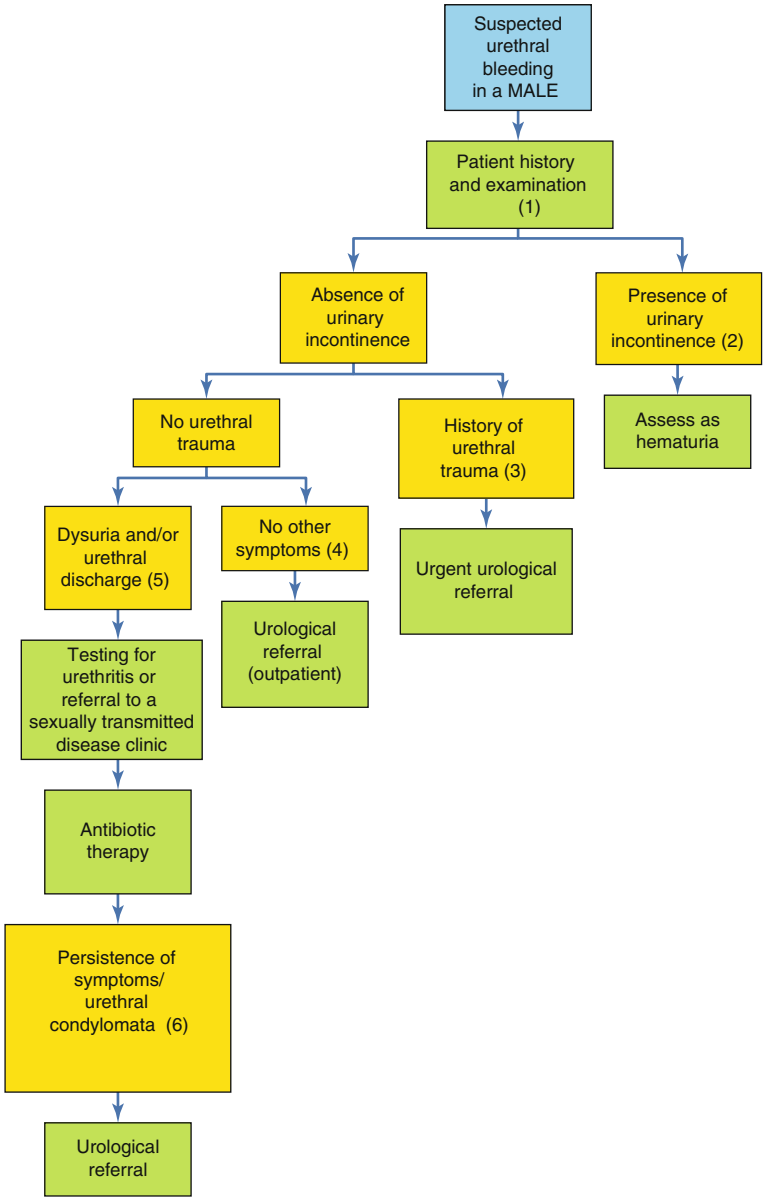
Table 10.1 Most commonly identifiable causes of urethral bleeding and clinical characteristics based on patient's history and examination

Sex	Disease	Patient's history and/or symptoms	Examination findings
Male	Urethral trauma[a]	History of blunt trauma to the bulbar urethra (straddling an object, kick in the perineum, unusual sexual or masturbation practices, in association with penile fracture), failed attempt at catheterization	Perineal and/or penile bruising/hematoma, urine retention
	Urethritis	Patient's reported sexual behavior at risk for sexually transmitted diseases and/or urethral discharge, dysuria	Urethral discharge on inspection or during milking of urethra
	Condylomata[b]	Usually painless, occasionally dysuria	Warts at the external urethral meatus
	Urethral tumors	(Rare), dysuria, obstructive urinary symptoms	Palpable urethral hardness or nodules
	Calculus impacted in the urethra	History of renal colic, dysuria, obstructive urinary symptoms, acute urinary retention	Palpable induration, circumscribed at a specific level of the urethra, usually painful
Female	Urethral caruncle[c]	Elderly, intermittent bleeding, occasionally dysuria, feeling of a lump at the urethral meatus	Polypoid, reddish lump, highly vascularized, located at the external urethral meatus
	Urethral diverticulum	Terminal dribbling, dysuria	Soft palpable bulging on the urethral surface
	Urethral tumors	(Rare), dysuria, obstructive urinary symptoms	Palpable urethral hardness or nodules

[a]Major urethral trauma involving pelvic fracture and thus located at the level of the posterior urethra is usually managed in an emergency department, in the context of a polytraumatized patient, and thus these patients are unlikely to be seen in the GP's office. Occasionally a male patient may come to the GP's office complaining of urethral bleeding after a blunt traumatic injury to the urethra, which occurred while straddling an object or as a consequence of a kick in the perineum. The possibility of unusual masturbation practices should always be kept in mind. Psychiatric patients may self-injure their penis or urethra using penetrating objects. It is essential to find out whether the patient has been able to spontaneously void his bladder. Inability to do so in the presence of a strong desire to urinate is highly suggestive of a urethral fracture (partial or complete). A butterfly perineal hematoma (this may not be present at the beginning but will rather manifest itself only the following day) is a further confirmation of a urethral injury. In this situation, any attempt to insert a transurethral catheter should be left to the specialist and preferably in an A&E context due to the high risk of misplacing it in a "false" urethral passage. If the patient is in pain because of urine retention, insertion of a suprapubic catheter represents a safer alternative

[b]Genital warts (condylomata) are viral sexually transmitted diseases presenting as villous growths usually located at the level of the glans and/or foreskin. Occasionally the disease can occur at the level of external meatus or fossa navicularis. Dysuria usually accompanies this presentation. Diagnosis and treatment consist of urethroscopy with electrocoagulation or laser coagulation of the villous growths

[c]Urethral caruncles are benign fleshy outgrowths at the urethral meatus, occurring primarily in postmenopausal women. They are generally thought to result from prolapse of a distal segment of the urethral mucosa probably as a consequence of estrogen deficiency. Histologically, they contain a core of blood vessels surrounded by hyperplastic transitional or squamous epithelium, hence their propensity to bleed



Flowchart 10.1 Urethral bleeding in the male

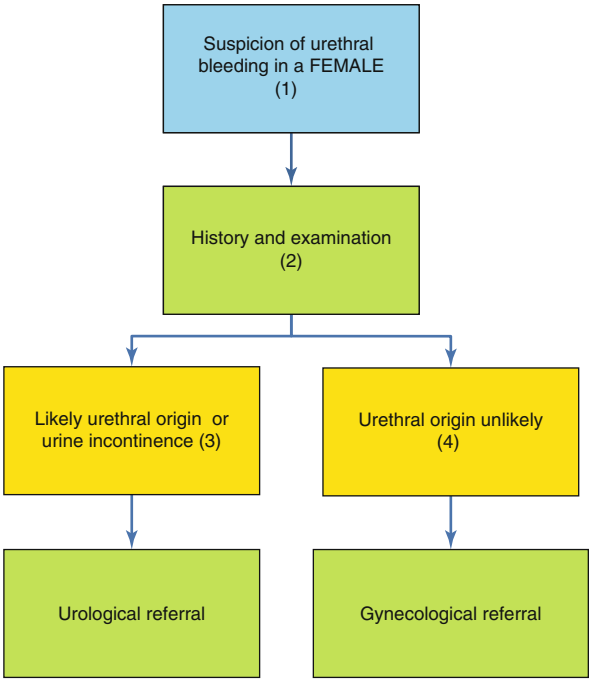
dysuria, frequency, difficulty in passing urine, and so on). Discussing sexual history will help to know whether to suspect sexually transmitted diseases. Inspection of the external genitalia is aimed at excluding penile or perineal hematomas (suggestive of trauma), ulcerations on the genital skin, and lesions of the glans

and the urethral meatus. Milking of the urethra allows the GP to exclude the presence of urethral discharge. Indurations or nodules at the level of penile and bulbar urethra can be felt with palpation.

2. If patient has a history of urinary incontinence, it may be difficult to ensure that the blood staining the pad or seen coming out of the urethra is not actually originating from the urinary tract above the urethral sphincter. In this case, the presence of hematuria cannot be ruled out and the patient should be investigated accordingly (see chapter on macroscopic hematuria).
3. If urethral bleeding is the consequence of a urethral injury, some degree of urethral disruption has occurred. The possibility of self-inflicted urethral trauma by psychiatric patients or as a consequence of masturbation practices should always be suspected. It is imperative to refer the patient to the A&E unit, particularly when urinary difficulties or penile and perineal hematoma are associated. Any suspicion of the presence of foreign bodies in the urethra or the bladder can be ruled out with a simple X-ray of the pelvis. Conservative management without hospital referral can be adopted in cases of minimal and rapidly self-resolving bleeding with no urinary difficulties. The patient should be counseled on the significant risk of developing a urethral stricture following any urethral trauma accompanied by urethral bleeding.
4. When urethral bleeding is not accompanied by other symptoms, no traumatic event is reported, and no sign of urethral diseases can be found during examination, the patients should firstly be reassured. The cause of the disease will most probably remain unknown. A urological referral is however wise to rule out the rare occurrence of a urethral polyp or urethral carcinoma by an endoscopic evaluation of the urethra (urethroscopy).
5. Dysuria associated with urethral discharge leads to the suspicion of urethritis. Testing for gonorrhea, chlamydia, and gram stain for gram-negative diplococci and polymorphonucleates is recommended. This can be done on a sample of urethral discharge obtained through urethral milking or endourethral swab. Chlamydia is currently more accurately detected via a nucleic acid amplification test on a sample of the first-catch urine. Alternatively, patient with suspected urethritis can be referred to a sexually transmitted disease clinic.
6. Persistence of urinary symptoms and urethral bleeding after antibiotic therapy warrants a urological referral. The same applies to condylomata detected at the urethral meatus, which are usually managed with endoscopic evaluation of the urethra, biopsy for viral subtyping and fulguration.

Comments About Flowchart 10.2

1. The diagnostic algorithm in cases of suspected urethral bleeding in a female can be extremely simplified, focusing on deciding the most appropriate specialist for referral.
2. History and examination of the patient should be oriented to determining whether the bleeding is more likely to be due to a urethral disease or has a genital (uterus, vaginal, or vulvar) origin. The female urethral meatus should be carefully inspected



Flowchart 10.2 Urethral bleeding in the female

for the presence of urethral caruncles or urethral polyps. Any abnormality of the whole urethra can be felt by digital inspection of the anterior vaginal wall. A lump or induration of the urethral contour suggests a urethral origin. Vulvar inspection and digital examination of the vagina and cervix can help to identify genital sources of bleeding.

3. Any abnormality during the inspection of the urethral meatus or following digital examination of the anterior vaginal wall warrants a urological referral. A urethral caruncle usually presents as a reddish, soft, polypoid growth protruding from the urethral meatus. Urethral diverticula or paraurethral cysts (arising from embryological Mullerian remnants) are not uncommon findings and usually appear as lumps bulging from the urethra, with a regular surface and of soft consistency. Primary or metastatic urethral neoplasms are rare and appear as irregular, hard alterations of the urethral profile. Incontinent patients, like their male counterparts, should be investigated for hematuria to rule out the possibility of bleeding from the urinary tract. Bleeding from the urethra may often be associated with various urinary symptoms, unlike genital bleeding.
4. When history and examination of the patient are in keeping with a low probability of urethral origin of the bleeding (no urinary symptoms with a normal-looking urethral meatus and absence of palpable urethral abnormalities in a continent patient), it may be reasonable to refer the patient to the gynecologist in the first instance. This is particularly true when a genital source of bleeding is clearly demonstrated.

Conclusions

Urethral bleeding is a urological symptom to be managed with a careful history-taking and a scrupulous clinical examination in the GP's office. By doing so, the majority of identifiable underlying etiologies can be suspected. The rare possibility of a urethral malignancy should always be kept in mind. It is advisable to refer most male patients to the urologist. The choice of the most appropriate specialist referral for the female patient – urological or gynecological – depends very much on the findings of the genital examination.

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Chapter 11
Hemospermia

Paolo Gontero

Abstract Hemospermia is not an uncommon clinical condition that can affect elderly patients as much as younger patients. In spite of the great anxiety generated in the patient, it is usually benign and rapidly self-resolving. In the majority of cases, the chance of an underlying life-threatening condition such as a malignancy is usually very low and mostly restricted to males over the age of 40. This age group needs a specialist referral for further investigations that aim to exclude prostate cancer. Conversely, in patients under 40, an infection in the urogenital tract is recognized as the most common etiological factor, and this can be safely assessed and treated by the GP. In this age group a urological referral is not necessary unless the symptom persists. Hemospermia can be accompanied by hematuria, a situation that warrants further investigation at any age. The etiology of the majority of hemospermia cases will ultimately remain unknown. A practical algorithm to guide the GP in the management of hemospermia is provided in the present chapter along with indications of when specialist referral is needed.

Keywords Hemospermia • Algorithm • Malignancy • Idiopathic • Post-traumatic • Dysuria • Urological referral

Introduction

Hemospermia, also termed hematospermia, is defined as the presence of blood in the semen. It is a fairly common condition that peaks between the ages of 30 and 40 years. Usually it is totally asymptomatic. Sometimes it can be associated with

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painful ejaculation, dysuria, urinary frequency, or scrotal pain. In most cases hemospermia is limited to one or two episodes, but occasionally it can present as a persisting and/or recurring condition. Particularly in this latter situation, the affected men and their partners fear the possibility of an underlying dangerous condition. By contrast, hemospermia is usually a benign condition and in most cases it is of unknown origin. However, some investigations are necessary as it can be a presenting symptom of urological disease, especially in men over 40 years of age.

Blood in the semen can arise from any disease occurring at any site along the route that the sperm travels within the male reproductive system, from its origin in the testicle, moving through the epididymis, the vas deferens, the prostate (where it also receives the seminal vesicle component) up to the urethra where it is discharged at the level of the external meatus.

The aim of the present chapter is to provide a practical algorithm for the management of this condition that can, in most instances, be handled by the GP.

Hints to Make a Diagnosis of Hemospermia

When taking the *patients*' *history*, attention should be paid to the frequency of the episodes and to the appearance of the blood that stains the sperm. Uniformly blood-stained sperm may suggest the prostate or seminal vesicles as the site of origin of bleeding. By contrast, the presence of blood clots within sperm that otherwise maintains its normal aspect suggests that the bleeding more probably occurred at the level of the urethra. Brownish stained sperm suggests a non-recent, self-resolved bleeding that occurred at the level of the prostate or seminal vesicles; it may, however, take even several weeks before the sperm clears completely. The presence of sperm stained with red blood is in keeping with recent bleeding. Sexual partners can be the source of blood (e.g., as a product of menstruation or cervical cancer), so it is important to question the patient on the circumstances when hemospermia was noticed. Exposure to tuberculosis, travel to areas in which schistosomiasis is endemic, and use of medications (especially anticoagulants or aspirin) should also be assessed as potential causes of bleeding within the spermatic route. Hemospermia is a very common complication of prostate biopsy, usually asymptomatic and self-resolving within a few weeks without treatment. Urethral instrumentation and prostate radiotherapy or brachytherapy can also cause hemospermia that, if persistent, warrants urological referral.

The *examination of the patient* should focus on the organs of the male reproductive system that are amenable to manual assessment, i.e., testicle, epididymis, the scrotal portion of the vas deferens, the prostate (through digital rectal examination), and the urethra (particularly the external meatus that should always be inspected).

The most common *causes of hemospermia* are reported in Table 11.1. These are urogenital infections, including prostatitis which can be implicated in up to 20 % of cases of hemospermia. Notably, malignancy was detected in only 3.6 % out of 859 cases of hemospermia. Only two cases were found below the age of 40 in 1 series,

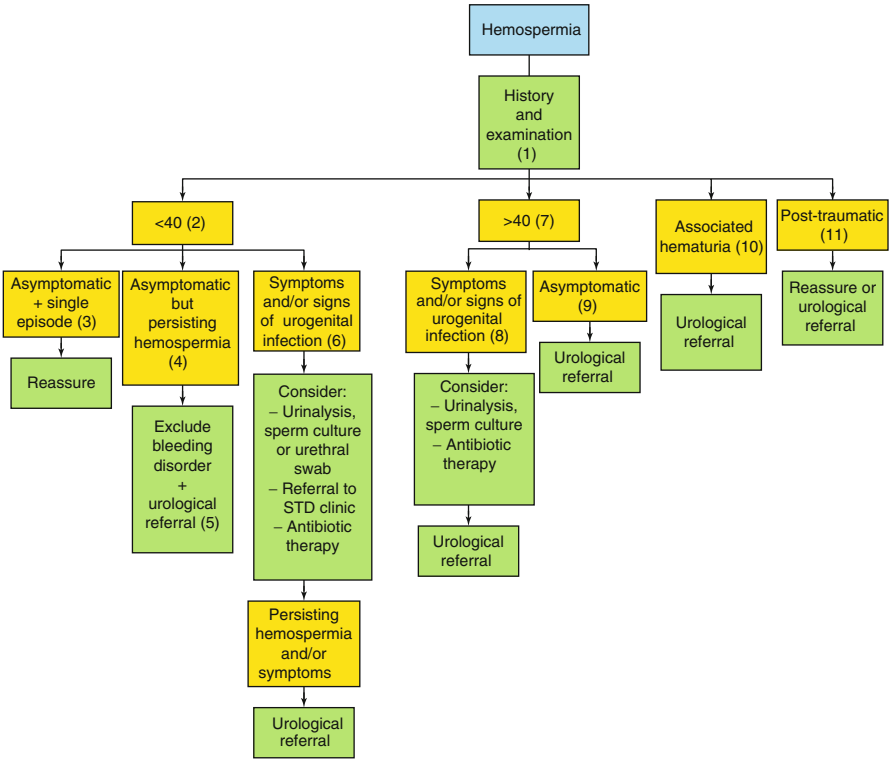
Table 11.1 Most common causes of hemospermia, their particular presentation symptoms, and findings during examination of the patient

Disease		Patient's history and symptoms	Examination findings
Prostatitis, seminal vesicle infection	25 %	History of prostatitis, current dysuria, and urinary frequency	Painful prostate during digital rectal examination
Epididymitis		Sexually transmitted diseases in young; symptomatic benign prostatic enlargement in adult/elderly	Tender epididymal mass
Urethritis		Young patients (history of sexually transmitted diseases)	Urethral discharge, dysuria
Malignancies (prostate cancer, seminal vesicle cancer)[a]	3 %	Age>40	Firm prostate during digital rectal examination
Venous varicosities (of prostate, bladder neck) or vascular abnormalities[b]	Undetermined	Usually accompanied by hematuria; in young patients, may be due to rare prostate hemangioma	Enlarged prostate on digital rectal examination. Hematuria can follow ejaculation
Post-traumatic hemospermia	–	Recent prostate biopsy, urethral instrumentation, radiation therapy to the prostate	Urethral bleeding or hematuria can be associated; prostate examination can be unremarkable
Bleeding disorders	Undetermined	Severe uncontrolled hypertension, any congenital or acquired disease causing bleeding diathesis	Splenomegaly, skin petechiae, hematuria
Idiopathic hemospermia[c]	68 %	–	Negative

[a]Since the sperm is released by the ejaculatory ducts at the level of the verumontanum, a portion of the anterior urethra that is covered by urothelium as well as some portions of the prostatic ducts, hemospermia may signal the rare occurrence of a transitional cell carcinoma involving either the prostatic ducts or the verumontanum

[b]During ejaculation the smooth prostatic sphincter undergoes contraction. When venous varicosities are present at the periprostatic or bladder neck level, this physiological function may provoke bleeding from these veins. Hematuria is likely to occur during the micturitions that follow ejaculation

[c]In the majority of cases, the cause of hemospermia will remain undetermined due to the difficulty in identifying an underlying disease as the pathogenetic cause of an isolated episode of hemospermia



Flowchart 11.1 Management of hemospermia in general practice

whereas in other series no malignancy was detected below the age of 40. Most of the malignancies are prostate cancer. In fact, hemospermia is an extremely rare accompanying sign in prostate cancer (0.5 %). Other forms of malignancies associated to hemospermia, such as seminal vesicles tumors or testicular tumors, are extremely rare. In the vast majority of cases (68 %), the cause of hemospermia remains unknown.

Management of Hemospermia in the GP's Office

Comments About Flowchart 11.1

1. Hints for history taking and examining a patient with hemospermia have been already discussed in point 2 of the present chapter (Hints to Make a Diagnosis of Hemospermia). One of the most useful categorizations is to distinguish between hemospermia patients in two age groups using the cutoff age of 40.
2. Males below the age of 40 are extremely unlikely to harbor an underlying malignant disease.

3. Asymptomatic patients with one or two episodes that self-resolve do need further investigations and can be reassured.
4. Persistent hemospermia, defined as continuous or recurrent bouts, in the absence of accompanying symptoms, indicates the need for further investigations irrespective of the patient's age. These should concentrate on excluding major bleeding disorders by asking for full blood count and a coagulation test followed by specialist referral in case of abnormal findings. More than half of hemospermia cases persist beyond 1 month, thus causing significant stress. The patient should be reassured on the more likely benign origin of the condition, although a urological referral is advisable.
5. In young patients, persisting asymptomatic hemospermia may also indicate the need to exclude congenital or acquired benign abnormalities of the prostate (Müllerian duct cysts, calculi) or the seminal vesicles (cysts) by means of a transrectal ultrasound, an effective first-line investigation that can be used to visualize the seminal vesicles, ejaculatory ducts, and prostate complex. In selected cases, MRI using an endorectal coil can help to elucidate the level of origin of bleeding within the seminal vesicles or the prostate.
6. When hemospermia is associated with dysuria, urinary frequency, and painful ejaculation, a urogenital infection is likely to be implicated. Examination may reveal a swollen epididymis (suggestive of an epididymitis), a painful prostate on digital rectal examination (consistent with prostatitis), or a urethral discharge (indicative of urethritis). Culture and microscopy of seminal fluid and of prostatic fluid collected during prostatic massage or of urethral smear can help to identify the infectious or inflammatory cause of prostatitis and urethritis, respectively. Irrespective of whether specific bacteria are identified or not, an antibiotic treatment is indicated in any case. In patients younger than 40, the prescribed antibiotic should be effective against chlamydia and gonorrhea; a 2-week course of oral ciprofloxacin or doxycycline is usually adequate. The GP may consider referral of patients with persistent symptoms to a sexually transmitted disease (STD) clinic or to urological care.
7. Any patient older than 40 should be preferably sent for a urological referral in order to exclude the possibility of prostate cancer or of other rare types of neoplasms.
8. In patients whose symptoms suggest prostatitis, specialist referral should be preceded by culture and microscopy of urine and seminal fluid or of prostatic fluid collected during prostatic massage. A 2-week course of oral ciprofloxacin should be suggested if all culture tests are negative. A delayed urological referral is advisable even if symptoms resolve since prostate cancer can coexist with prostatitis. It should be kept in mind that a PSA test performed in presence of prostatitis may generate a false-positive result.
9. Males aged over 40 with asymptomatic hemospermia warrant a urological referral. Specialist care will essentially focus on excluding prostate cancer by performing PSA testing, digital rectal examination, and transrectal ultrasound as first-line assessment.
10. When hemospermia is associated with hematuria, the patient should also be investigated to exclude malignancies that can present with a combination of

these two signs, such as a transitional cell carcinoma of the prostatic urethra. Urine cytology and bladder ultrasound are mandatory first-line investigations, followed by urological referral for cystoscopy.

11. Patient's history should always aim to exclude a traumatic origin of hemospermia. Nowadays hemospermia following prostate biopsy has become a fairly common situation due to the widespread diffusion of prostate biopsy as a result of PSA testing. This condition does not require specific treatment nor specialist referral. Patients should be advised that it may take several weeks before hemospermia disappears. Other potential sources of post-traumatic hemospermia include urethral instrumentation, testicular injury, or perineal trauma that can be referred to specialist care according to the severity of injury.

Conclusions

The most important intervention of the GP in the presence of hemospermia, after careful history taking and examination, is to reassure the patient since the risk of malignancy is rare. Then the proposed decision-making algorithm can be used. Patients over the age of 40, or any patient with persisting asymptomatic hemospermia or associated hematuria, benefit from a urological referral. Patients under 40 and with a rapidly self-resolving hemospermia can be safely discharged without further investigations. Hemospermia accompanied by symptoms suggestive of urogenital infection should be assessed to identify the causative infection and treated accordingly: persistent symptoms indicate the need for a urological referral.

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Chapter 12
Genitourinary Fever in Adults

Paolo Gontero

Abstract Since a broad spectrum of urological diseases may present with fever, the presence of this symptom, particularly when accompanied by features suggesting an acute infection (high temperature, rapid onset with shivering), must prompt the search for a urological origin. The location of the site of infection can be relatively straightforward when a fever is accompanied by specific symptoms or signs: the association with loin pain and a tender kidney usually indicates an infection of the kidney or the upper urinary tract; a painful and swollen scrotum is consistent with an epididymo-orchitis, while suprapubic pain and dysuria together with a high temperature suggest acute prostatitis.

The aim of this chapter is to provide a practical algorithm to promptly detect the possible urological origin of a high temperature and to guide its initial management. A careful history and patient's examination is usually sufficient to identify the site of origin of a urogenital infection. Immediate outpatient antibiotic treatment or hospital referral are based on the severity of the clinical situation.

Keywords Fever • Urogenital infection • Prostatitis • Epididymitis • Orchitis • Pyelonephritis • Sepsis • Urosepsis

Introduction

Since a broad spectrum of urological diseases may present with fever, the presence of this symptom, particularly when accompanied by features suggesting an acute infection (high temperature, rapid onset with shivering), must prompt the search for a urological origin. At the other end of the spectrum, a significant proportion of fevers

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Table 12.1 Initial diagnostic hints that help to diagnose a genitourinary fever

Action	Finding	Comment
Inspection of urine sample	Cloudy appearance	Usually suggests pyuria
	Smelly urine	Usually suggests an infection
Urine dipstick	Leukocytes and/or nitrates and/or alkaline pH	Indicative of UTI
History	Recent urological maneuvers	Risk factor for urosepsis
	Diabetes	Risk factor for complicated UTI
	Indwelling catheter	Risk factor for complicated UTI or urosepsis
	Compromised immune system	Can predispose to UTI/urosepsis
	Pregnancy	Can predispose to ascending UTI
	Bimanual kidney palpation	Pain suggests a kidney infection
	Suprapubic inspection	Pain is suggestive of prostatitis
	Scrotal examination	Enlarged and tender epididymis/testicle is suggestive of epididymitis/orchitis
	Digital rectal examination	Prostate tenderness is suggestive of prostatitis

initially considered of unknown origin are in fact of urological origin. Generally, a fever of urogenital origin indicates that an infection has involved either the tissue or the parenchyma of the relevant organs. A simple cystitis is in fact usually afebrile.

The location of the site of infection can be relatively straightforward when a fever is accompanied by specific symptoms or signs: the association of loin pain and a tender kidney usually indicates an infection of the kidney or the upper urinary tract; a painful and swollen scrotum is consistent with an orchiepididymitis, while suprapubic pain and dysuria together with a high temperature suggest acute prostatitis.

Urogenital infections can be complicated by sepsis, a clinical picture characterized by infection accompanied by signs of systemic inflammation (fever or hypothermia, tachycardia, tachypnea, leukocyturia, or leukopenia). A septic fever is a life-threatening condition that can progress to septic shock and therefore needs to be promptly recognized. In this respect, patients with an indwelling catheter or with severe obstructive lower urinary tract symptoms are considered at risk of developing such an infection.

This chapter provides an algorithm to promptly detect the possible urological origin of a high temperature and to guide its initial management.

Hints to Identify a Fever of Urological Origin

The majority of urogenital fevers originate from infected urine that enters the blood stream, thus causing a bacteremia. Table 12.1 lists symptoms, signs, and urine dipstick findings that should be looked for to diagnose febrile urinary tract infections (UTI) or, more generically, a genitourinary fever.

Table 12.2 Upper urinary tract diseases that present with a genitourinary fever

Disease	Suggestive history	Findings on examination
Acute pyelonephritis[a]	Known vesicoureteral reflux, diabetes, recent endoscopic urological maneuvers. Typical presentation: high temperature, flank pain/renal colic, nausea, and vomiting	Marked tenderness when examining the kidney, abdominal distension, Blumberg sign sometimes positive (thus mimicking peritonitis) Leukocytes on urine dipstick
Chronic pyelonephritis[b]	Previous recurrent episodes of pyelonephritis can be recalled. Usually mild symptoms, fever can be absent	Kidney examination and urine dipstick can be both unremarkable. Signs of chronic renal failure when the disease is bilateral
Pyonephrosis[c]	Known upper urinary tract obstructive diseases (i.e., calculi)	Kidney mass tender on palpation
Renal abscess[d]	Compromised immune system	Tender kidney
Perirenal abscess[e]	Symptoms can be mild with general malaise, asthenia, mild temperature	Kidney mass, reddish cutaneous bulging, cutaneous fistula

[a]Acute pyelonephritis is an infection involving the renal parenchyma. It can result from an ascending urine infection (from bacteria usually found in UTI) in presence of a vesicoureteral reflux or urological endoscopic maneuvers, or develop from the localization within the kidney of a systemic infection. Patients with a higher predisposition to UTI (e.g., diabetics) have a higher risk of developing pyelonephritis

[b]Recurrent episodes of acute pyelonephritis with persistence of predisposing factors can lead to chronic pyelonephritis, a progressive fibrosis of the renal parenchyma with progressive loss of kidney function

[c]Any blockage of the upper urinary tract due to obstruction in the presence of infected urine (e.g., infected stones) can be defined as pyonephrosis

[d]In an immunocompromised patient or in a patient who is diabetic or undergoing hemodialysis, a bacteremia arising from the cutaneous Staphylococcus aureus can determine the formation of microabscesses at the renal cortex that can fuse together to develop one or more renal cortical abscesses. The most frequent form of renal abscess is the renal corticomedullary abscess that can originate from an ascending urine infection in a patient with *E. coli* UTI and a vesicoureteral reflux

[e]A perirenal abscess is usually the result of a rupture of a renal abscess in the perirenal space

Tables 12.2 and 12.3 list the main diseases of the upper and lower urinary tract respectively that may present with a genitourinary fever.

Table 12.3 Lower urinary tract diseases that most frequently cause genitourinary fever or urosepsis

Disease	History	Findings during examination
Acute bacterial prostatitis[a]	High temperature with shivering, suprapubic and/or perineal pain, painful micturition	Enlarged, hot, and tender prostate during digital rectal examination. Urine dipstick can show leukocytes
Prostatic abscess	Previous episodes of acute prostatitis, recent prostate biopsy, high temperature	Sensation of "fluctuation" of the prostate surface during digital rectal examination
Acute epididymitis[b]	Exposure to sexually transmitted diseases. Scrotal pain, developing progressively over several hours	Enlarged, hard-feeling, and heavily tender epididymis and/or testicle, reddish scrotal skin
Testicular abscess[c]	History of previous epididymitis can be associated with sepsis	Scrotal skin edematous and reddish. A sensation of "fluctuation" of the scrotal content can be felt during examination. Possible scrotal skin fistula with spontaneous drainage of the abscess
Mumps orchitis[d]	Glandular swelling and pain in the jaw area usually appearing 1 week earlier. Mild to severe testicular pain, lower abdominal pain	Scrotal edema with reddish scrotal skin. Testicle appears enlarged and tender on examination, while epididymis appears normal

[a]Acute bacterial prostatitis is an acute infection of the prostate mainly caused by gram-negative bacteria (essentially E. coli and pseudomonas). An infection ascending from the urethra is the most common route of transmission. Microorganisms in the urine may also enter the prostatic ducts against the regular flow of urine. Finally, bacterial prostatitis may also arise through direct infiltration of the rectal bacteria. Acute bacterial prostatitis can develop into a prostatic abscess.

[b]Acute epididymitis is a bacterial infection of the epididymis. In young men, the infection can be due to a sexually transmitted infection from chlamydia or gonorrhea and is associated with urethritis (inflammation of the urethra). In older men over 40, it is associated with urinary tract infections and prostatitis. It is believed to be caused by the retrograde passage of urine from the prostatic urethra to the epididymis via the ejaculatory ducts and vas deferens. When the infection is severe and extends to the adjacent testicle, it is termed acute epididymo-orchitis. A testicular abscess can occur in up to 5 % of cases.

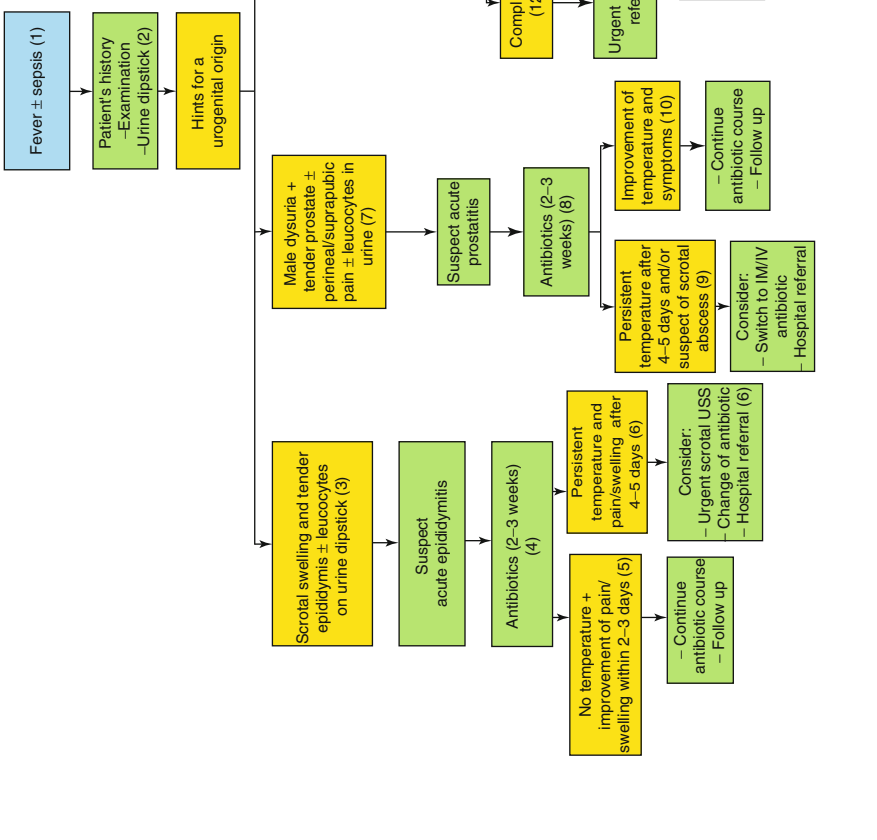
[c]A testicular abscess is usually a complication of severe epididymo-orchitis. The majority of patients develop a testicular abscess as a result of untreated or severe epididymo-orchitis. If the abscess ruptures through the tunica albuginea, then a scrotal abscess may develop. In most cases epididymo-orchitis has been present for some time, and thus typically patients present with testicular pain, often accompanied by fever and swelling, which has lasted a number of days.

[d]Mumps orchitis is the most common male testicular infection that can affect up to 30 % of adults with mumps. Orchitis usually manifests a few days after clinical evidence of mumps, thus making the diagnosis fairly straightforward.

Diagnosis and Management of a Genitourinary Fever in the GP's Office

Comments About Flowchart 12.1

1. Any patient presenting with fever, with or without an associated sepsis, should always be assessed in order to rule out the possibility of the fever having a genitourinary origin.
2. Patient's history should focus on identifying risk factors and genitourinary symptoms suggestive of an infectious colonization of the genitourinary tract. Patient's examination should always include the external genitalia and a digital rectal examination as well as an examination of the kidneys.
3. A scrotal swelling in the presence of a tender and hard epididymis is highly suggestive of acute epididymitis. The spermatic cord is usually tender and swollen. In young patients the possibility of a testicular torsion must always be kept in mind: testicular torsion is not usually febrile unless there is testicular necrosis.
4. While it is advisable to send a urine sample for culture, it is not necessary to wait for the results; rather, an antibiotic therapy should be started promptly. Antimicrobials should be selected on the empirical basis that in young, sexually active men, *C. trachomatis* is usually causative, and in older men with BPH or other micturition disturbances, the more common uropathogens are involved. Fluoroquinolones, preferably those with activity against *C. trachomatis* (ciprofloxacin and levofloxacin), should be the drugs of first choice because of their broad antibacterial spectra and their favorable penetration into the tissues of the urogenital tract. Treatment should last 2–3 weeks. For young men, epididymitis can lead to permanent occlusion of the epididymal ducts and thus to infertility. For this reason antiphlogistic therapy with corticosteroids may be considered.
5. Treatment response is indicated by resolution of the high temperature and improvement of local symptoms within 3–4 days. Patients should be advised that the hard and enlarged epididymis may last for at least 1 month in spite of adequate therapy.
6. Persistence of a high temperature beyond 3–4 days after treatment suggests a switch to IM or IV antibiotics (3rd-generation cephalosporins or aminoglycosides are both valid options) and a scrotal ultrasound to rule out a scrotal abscess. Compromised clinical conditions warrant hospital admission.
7. In a male, fever associated with urgency and dysuria is highly suggestive of acute prostatitis. Finding a tender prostate during the digital rectal examination usually confirms the diagnosis.
8. An oral antibiotic such as trimethoprim or fluoroquinolone can be the initial choice. An NSAID can be used for analgosia.
9. Persistence of temperature after 3–4 days suggests inadequate treatment. The possibility of a scrotal abscess, which needs to be drained, should be ruled out. A switch to IM or IV antibiotics (3rd-generation cephalosporins or aminoglycosides) or hospital referral should be considered.
10. Resolution of fever within 2–3 days suggests treatment response to oral antibiotics. On the contrary, urinary symptoms may persist for longer. Treatment should then be continued for up to 2–3 weeks.



Flowchart 12.1 Management of a presumed genitourinary fever

11. Temperature associated with flank pain/renal colic (usually unilateral, rarely bilateral) is highly suggestive of a kidney infection. Cystitis-like symptoms and the presence of leukocytes on the dipstick strengthen the diagnosis. The most common situation is acute pyelonephritis although the other more complicated, though rare, types of kidney infection reported in Table 12.2 must always be taken into consideration.
12. All complicated kidney infections should be referred to the hospital for inpatient treatment. This applies to one or more of the following situations: diabetes, pregnancy, recent surgery or urological procedure, immunosuppression/kidney transplant, known history or clinical suspicion of calculi and/or hydronephrosis, elderly and frail patients, or those showing signs of sepsis.
13. In the absence of complications, patients in an otherwise good clinical condition may be amenable for outpatient management.
14. It is imperative that an antibiotic therapy is started immediately. While a urine sample must be sent for culture, there is no time to wait for the results; therefore, the choice of an antibiotic will be empirical. Oral fluoroquinolones administered at full dose have proved effective. In the absence of solid data on the optimal treatment duration, it is advised that patients continue the therapy for up to 2 weeks. IM administration of 3rd-generation cephalosporins or aminoglycosides for 1 week is an alternative option.
15. If the clinical conditions and in particular the fever do not show significant improvement within 24–48 h, it is likely that a complicated infection is present and the treatment is inadequate. The patient should therefore be referred to the hospital for urgent investigations and IV antibiotics.
16. Remission of temperature within 48–72 h suggests that the antibiotic is effective. The treatment should preferably be continued for up to 2 weeks. Urine culture should be repeated after treatment and the upper urinary tract investigated with an ultrasound. Patients may be referred for an outpatient urological appointment.
17. An indwelling catheter should always be suspected as the source of a fever. Occasionally the patient complains of symptoms suggestive of a urinary tract infection (such us suprapubic pain, flank pain, or a burning sensation localized at the distal urethra). The presence of cloudy urine further confirms the suspicion.
18. It is advisable to send a urine sample for culture and to consider replacing the catheter if it has been in place for more than 1 week. An empirical course of a broad-spectrum antibiotic should be started. Antibiotics previously used for prophylaxis should be avoided because of the risk of resistance. Uroseptic fever is an indication for hospital admission.

Conclusions

The presence of a fever of unknown origin should always prompt the suspicion of a urogenital origin. Patient's history should focus on previous episodes of urinary tract infections, known congenital abnormalities of the urinary tract, and underlying conditions that may favor urogenital infections (urinary calculi, obstructive uropa-

thy, diabetes, and so on). Patient's examination should include the assessment of kidneys, and external genitalia, and digital rectal and vaginal examinations. A urine sample should always be immediately stored for urine culture testing.

A urogenital fever usually presents with a rapid onset, shivering, general malaise, and a high temperature. The potential evolution to urosepsis should always be taken into consideration, particularly in complicated cases and in elderly patients. Clinical situations such as acute epididymitis, prostatitis, and pyelonephritis or a catheter infection can usually be recognized by means of a careful history and examination. Immediate outpatient antibiotic treatment or hospital referral must be advised based on the severity of the clinical situation and the presence or absence of complications.

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Chapter 13
Male Lower Urinary Tract Symptoms

Mark J. Speakman and Jemima Scott

Abstract Lower urinary tract symptoms (LUTS) are the cause of considerable bother to our patients and impact greatly on patient quality of life. They are a commonly encountered complaint in primary care. Symptoms can be more obstructive, like hesitancy and poor flow, when they are called voiding symptoms and/or more irritative such as urgency and frequency when they come more from the storage phase of micturition. Increasing evidence shows that the majority of patients can be safely treated in primary care and that first-line treatment can be safely started after a good history, a focused examination, and a few basic investigations. Only when the risky "red flag" symptoms have been identified or when patients fail to respond to first-line therapy is a referral for specialist investigation required. All patients should be offered advice on lifestyle adjustments; a trial of conservative management alone with review at 6 months is appropriate if symptoms are not currently bothersome. In patients with bothersome symptoms, the first-line medical treatment is an alpha-blocker, which should be combined with a 5-alpha reductase inhibitor in the presence of risk factors for progressive disease. Second-line therapies may be added in at 6-week review.

Keywords Urinary tract • Prostate diseases • Drug therapy • Combination • Alpha-blockers • 5-Alpha reductase inhibitors

Introduction

The term "lower urinary tract symptoms" (LUTS) encompasses a range of irritative storage and obstructive voiding difficulties. The phrase is purposefully gender nonspecific and does not presume an anatomical site of origin for the symptoms. In males the most

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Table 13.1 Classification of LUTS

Storage	Voiding	Post-micturition
Frequency[a]	Slow stream	Post-micturition dribble
Urgency[b]	Splitting or spraying	Feeling of incomplete emptying
Nocturia[c]	Terminal dribble	
Incontinence	Intermittency	
	Hesitancy	
	Straining	

[a]Urinary frequency is the need to urinate more often than usual. The normal urination of asymptomatic people varies widely with fluid intake, age, and gender. It has been reported that the majority of men urinate an average of seven times daily

[b]Urgency is defined as an abnormal or inappropriate sudden desire to pass urine that is difficult to defer for fear of leakage

[c]Nocturia is defined as the need to wake up one or more times nightly to void with each void preceded and followed by sleep. Studies of the relationship between quality of life and nocturia suggest that the condition becomes clinically significant when two or more voids nightly are experienced

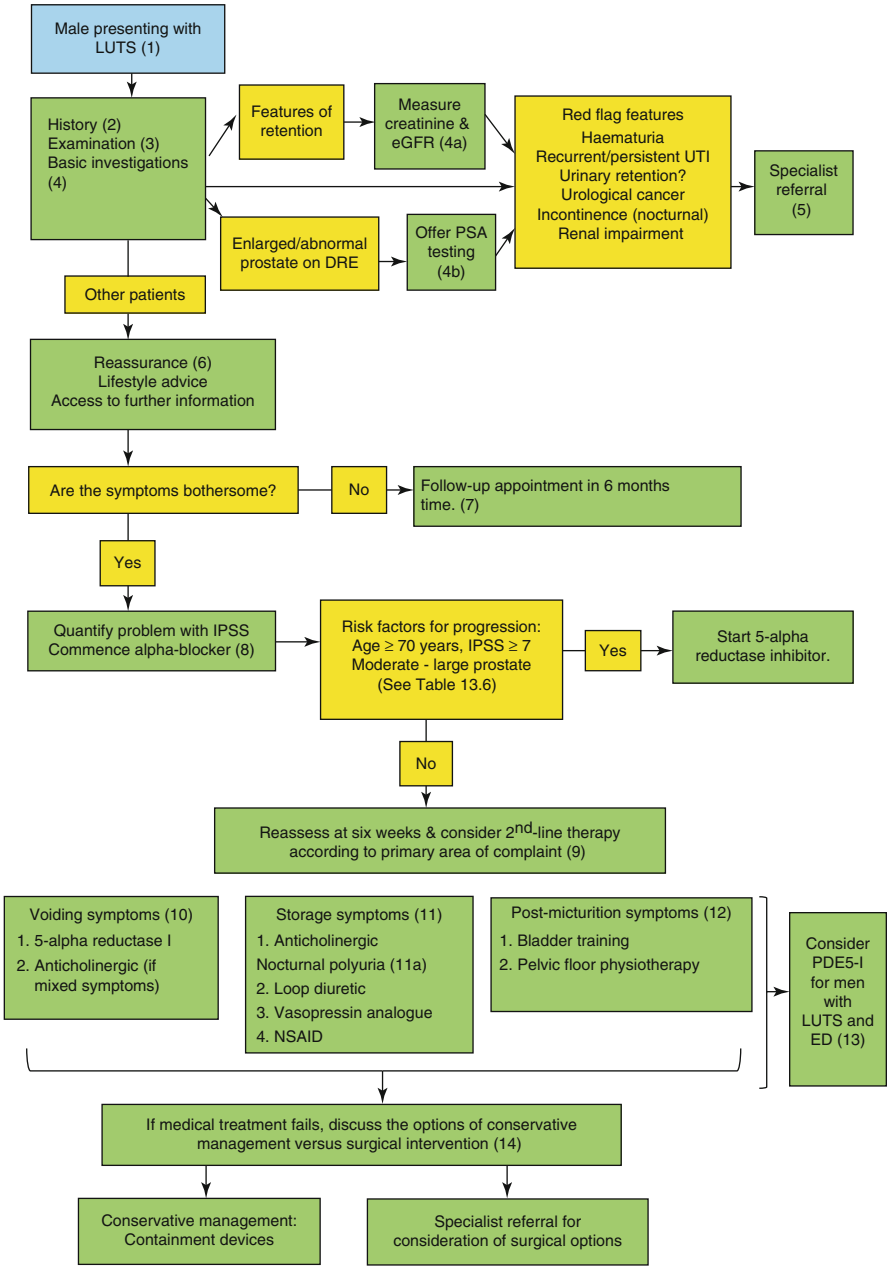
common cause is bladder outlet obstruction (BOO) secondary to enlargement of the prostate gland. Numerous other structural and functional disorders of the urinary tract as well as neurological and endocrine conditions can also present in a similar way and should be actively excluded during assessment.

The majority of patients presenting with LUTS can be appropriately and effectively managed in primary care. The aim of this chapter is to lay out a simple algorithm for the assessment and management of male patients presenting with voiding difficulties and to highlight the "red flag" features that should precipitate referral to a urology specialist. The algorithm is based upon categorization of the predominant complaint into storage, voiding, or post-micturition symptoms as reported in Table 13.1.

Investigation and Management of Males Presenting with Lower Urinary Tract Symptoms

Comments About Flowchart 13.1

1. Men with LUTS present to primary care for a variety of reasons. These include bothersome symptoms, fear about prostate cancer (PCa), or pressure from family members. Identifying this precipitant is key to an effective consultation.
2. The consultation should start with a history. Aim to determine the primary area of concern, voiding, storage, or post-micturition symptoms, as this will help subsequent management. Sexual dysfunction commonly overlaps with LUTS and should be enquired about specifically. Take a full drug history, including over-the-counter and herbal medications, and assess comorbidities.
3. Examine the patient as directed by the history but always including the abdomen, external genitalia, and digital rectal examination (DRE).
4. All patients with LUTS should have a urine dipstick test for leukocytes, nitrites, blood, glucose, and protein and be asked to complete a frequency-volume chart



Flowchart 13.1 Male presenting with LUTS

Table 13.2 Frequency-volume chart. Men should be asked to report on a sheet the time each micturition occurred and the volume of urine voided and to mention whether urgency or incontinence occurred over 3 consecutive days. The more complex the information collected, the poorer the compliance from the patient. The chart below provides a scheme for easily constructing a self-made table for data collection

	Day 1	Day 2	Day 3
Time	Volume/incontinence/ urgency	Volume/incontinence/ urgency	Volume/incontinence/ urgency
6 AM			
7 AM			
8 AM			
9 AM			
10 AM			
11 AM			
12 noon			

Continued

(Table 13.2). As well as quantifying LUTS (Table 13.3), this questionnaire can be of significant value in determining the underlying cause. It is of particular importance in patients with troublesome nocturia. Further investigations, including urine flow studies (uroflowmetry) and measurement of post-void residual (PVR), are generally only necessary in those patients who are being considered for second-line management.

4a. Any indication of chronic urinary retention should prompt measurement of the serum creatinine and eGFR. Suggestive features include nocturnal enuresis, recurrent urinary tract infection, or a palpable/percussible bladder. Patients with elevated creatinine require ultrasound scanning for hydronephrosis and specialist referral.

4b. Measurement of PSA is advisable in men with a clinically malignant DRE. In benign prostatic disease, a PSA > 1.4 g/dl equates to a prostate of approximately 30–40 cc, the size of a golf ball. Values greater than this suggest a high risk of progression, and such men should be managed more aggressively. Testing should be performed after appropriate counselling of the patient, including an explanation of false-negative and false-positive results.

5. Specialist referral is indicated in patients with abnormal test results or any other "red flag" features.
6. Patients presenting without "red flag" features can be effectively managed in primary care. All men should be offered advice on lifestyle measures (appropriate fluid intake and the reduction of caffeine, sweeteners, and alcohol) and given access to sources of further information and support. If relevant, offer containment devices such as pads and catheters.
7. If the LUTS are non-bothersome, conservative management with follow-up after 6 months would be entirely appropriate.
8. Patients with troublesome LUTS should firstly have their symptoms quantified with the IPSS questionnaire (Table 13.3). They should then be offered a trial

Table 13.3 International Prostate Symptom Score (IPSS)

	Never	<20 %	<50 %	50 %	>50 %	>90 %	Score
Incomplete emptying							
Over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5	
Frequency							
Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
Intermittency							
Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
Urgency							
Over the last month, how difficult have you found it to postpone urination?	0	1	2	3	4	5	
Weak stream							
Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
Straining							
Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	

	None	Once	Twice	3 times	4 times	≥5 times	Score
Nocturia							
Over the past month, how many times did you most typically get up to urinate from the time you went to bed until the time you got up in the morning?	0	1	2	3	4	5	

Quality of life due to urinary symptoms	Delighted	Pleased	Satisfied	Mixed	Dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?	0	1	2	3	4	5	6

Total score: 0–7 mildly symptomatic, 8–19 moderately symptomatic, 20–35 severely symptomatic

Table 13.4 Suggested lifestyle changes for male LUTS

Intervention	Rationale
Fluid restriction[a]	Reduces urine production and thus alleviates bothersome daytime frequency and/or nocturia. This is particularly advocated in patients found to have polyuria (24-h urine output >40 ml/kg) on the frequency/volume chart with no apparent underlying conditions known to cause polyuria (diabetes mellitus and diabetes insipidus). Patients with a nightly urine output >33 % of the total 24-h urine output are likely to suffer from nocturnal polyuria and may benefit from fluid restriction in the evening
Caffeine consumption reduction	Caffeine tends to act as an irritant to the bladder
Weight loss	A strong independent relationship between obesity and LUTS as well as benign prostatic hyperplasia has been demonstrated

[a]Excess fluid restriction (i.e., less than 1.5 l/day) should be avoided as concentrated urine may irritate the bladder as well as predispose to urinary tract infections

period of lifestyle adjustments (Table 13.4) and/or immediate active intervention. If the latter is chosen, the first-line treatment is an alpha-blocker (see Table 13.5 for further information on alpha-blockers). If the patient has risk factors for progressive disease (Table 13.6), they should be started on dual therapy with the addition of a 5-alpha reductase inhibitor (see Table 13.5 for further information on 5-alpha reductase inhibitors). To evaluate the efficacy of intervention, use the validated symptom score such as the International Prostate Symptom Score (IPSS) both at baseline and follow-up appointment (Table 13.3).

9. After 6 weeks, the effect of the alpha-blocker should be apparent and second-line therapy added in if required, according to the prime area of the complaint.
10. Persistent voiding symptoms such as hesitancy, straining, slow or intermittent stream, spraying, and terminal dribble may be helped by the addition of a 5-alpha reductase inhibitor like dutasteride or finasteride. Alpha-blockers and 5-alpha reductase can be used in combination as they have different mechanisms of action. Selective alpha-blockers reduce the tone of the prostatic and bladder neck smooth muscle. They are effective within 24–48 hours and can be used on an intermittent basis. 5-Alpha reductase inhibitors prevent the conversion of testosterone to potent dihydrotestosterone, thus removing the stimulus to ongoing hyperplasia of the prostate. They achieve a reduction in glandular volume of 20–25 % at 6 months and may also reduce the risk of malignancy by the same percentage. These drugs can be continued long term.
11. Persistent storage symptoms such as urgency, frequency, and urgency incontinence can be treated by the addition of an antimuscarinic drug. Urgency and nocturia are the most bothersome symptoms. Urgency is the abnormal or inappropriate sudden desire to pass urine that is difficult to defer for fear of leakage. A frequency-volume chart (Table 13.2) can help to differentiate simple nocturnal frequency from nocturnal polyuria, discussed in more detail below. The underlying pathophysiology of storage symptoms is thought to be an overactive

Table 13.5 Common drugs used in the management of LUTS

	5-Alpha reductase inhibitors[a]	Alpha-blockers[b]	Anticholinergics[c]
Indications	Bothersome LUTS in patients with BPE or risk factors for progression	Bothersome LUTS (any) Acute urinary retention	Storage symptoms (OAB); generally second line
Benefits	Reduced symptoms Reduced (a) risk of urinary retention, (b) need for surgery, and (c) risk of prostate Ca (off-license usage)	Rapid reduction in symptoms Delay in time to retention or need for surgery	Reduced urgency and frequency
Side effects	Erectile or ejaculatory failure in 5–10 % Take 3–6 months to work	Postural hypotension Retrograde ejaculation	Dry mouth and constipation. Increased risk of urinary retention in some patients
Contraindications		Must be stopped 1 month prior to cataract surgery	Patients with PVR >200 ml
Monitoring	At 3–6 months, then every 6–12 months PSA falls by 50–60 % at 6 months	At 4–6 weeks, then every 6–12 months	Add to alpha-blocker at 6-week review if required
Examples	Dutasteride 0.5 mg OD Finasteride 5 mg OD	Alfuzosin 10 mg OD Tamsulosin 400 mcg OD Doxazosin 4 mg OD (titrate dose)	Fesoterodine 4–8 mg OD Oxybutynin 2.5–5 mg BD–QDS Solifenacin 5–10 mg OD Tolterodine 4 mg OD

[a]The first-line treatment should be with an alpha-blocker in the majority of patients such as tamsulosin or alfuzosin. Clinical improvement should be seen quickly, and a review of symptoms is therefore indicated after about 6 weeks. Side effects to be aware of include postural hypotension and retrograde ejaculation, although these drugs are well tolerated by the majority. Alpha-blockers are associated with the development of intraoperative floppy iris syndrome during cataract surgery and should therefore be stopped for one month in advance and ophthalmic surgeons alerted

[b]5-Alpha reductase inhibitors should be considered for men with troublesome LUTS secondary to significant BPE (volume >40 cc and/or PSA >1.4 Ng/l) as well as those with more than two risk factors for disease progression. These drugs act by reducing prostate size (20–25 %) and therefore also PSA value (50–60 %) but can take up to 6 months to do so. In addition to improving LUTS, 5-alpha reductase inhibitors reduce the long-term risk of urinary retention, prostatic surgery, and prostate cancer. Men should be warned however that about 10 % experience erectile or ejaculatory failure

[c]Anticholinergic agents are effective at reducing storage symptoms due to an overactive bladder. The choice of patient is however important as these drugs have significant side effects, especially in the elderly. Avoid in those with significant BOO (post-void residual >200 ml), urinary retention, autonomic neuropathy, and closed-angle glaucoma. Typical antimuscarinic side effects may also limit their use; review the prescription at 4–6 weeks and then every 6–12 months

Table 13.6 Risk factors for progressive disease

Age ≥70 years
IPSS ≥7
Qmax ≤12 ml/s
Prostate volume >30–40 cc
PSA ≥ 1.4 ng/ml
Large residual volume (>150 ml)
Failure to respond to alphablockers

bladder (OAB), resulting from a functional and/or structural change in the detrusor muscle. OAB is defined as urgency with or without urgency incontinence usually associated with frequency and nocturia once urinary infection and other bladder pathology have been excluded. Anticholinergic agents reduce the parasympathetic stimulus to the bladder, providing significant symptomatic relief. They can carry an increased risk of urinary retention and are therefore generally used in combination with alpha-blockers. It is safer to avoid these drugs in patients with a post-void residual of >200 ml.

11a. Nocturnal polyuria occurs when the volume of urine produced overnight (including first void in the morning) is greater than 33 % of the total 24-h output. It is obviously important to exclude medical and endocrine causes of polyuria before starting treatment. Advising the patient to lie flat for an hour in the afternoon can reduce peripheral edema and hence nocturnal urine production. The options in terms of medical treatment are diuretics, vasopressin analogues, and low-dose nonsteroidal anti-inflammatories (NSAIDs), all of which should be used with caution. A loop diuretic such as 20 mg furosemide taken in late afternoon is first line. Vasopressin analogues such as desmopressin are a highly effective treatment for nocturnal polyuria but require careful monitoring of both blood pressure and serum sodium. A low-dose NSAID, such as ibuprofen 200 mg nocte, in patients without gastric symptoms may also be of benefit to selected patients because of the association of inflammatory pathways and nocturia.

12. Terminal dribble and the feeling of incomplete bladder emptying are categorized as post-micturition symptoms. Affected patients may benefit from bladder training, whereby the interval between voids is gradually increased over time, or pelvic floor physiotherapy. If these measures fail or immediate active intervention is desired, an alpha-blocker can be offered although these symptoms are notoriously difficult to improve with medical therapies.
13. A significant proportion of men presenting with LUTS have additional erectile dysfunction (ED), and this should be enquired about specifically. Phosphodiesterase inhibitors (PDE5- I) such as sildenafil, tadalafil, and vardenafil can be used in combination with alpha-blockers and have the added benefit of providing a modest improvement of LUTS, although in several countries they are not currently licensed for this indication alone.
14. A specialist referral is warranted in patients who continue to experience disruptive symptoms despite optimal medical therapy as well as those with recurrent

retention, repeated infection, or hematuria. At this point a careful discussion must be had as to whether the patient wishes to pursue surgical or conservative management. Surgical options depend upon the type and severity of underlying pathology as well as the patient's comorbidities. Surgical options include transurethral resection of the prostate (TURP), bladder neck incision (BNI) laser enucleation, or open prostatectomy.

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Chapter 14
Male Dysuria/Prostate Pain

Andrew Doble

Abstract In the assessment of male patients with dysuria or prostate pain, the initial search must be for causative organisms and specific sources of the symptoms. Chronic bacterial prostatitis (type II) is the commonest cause of urinary infection, but specific causes like bladder outflow obstruction or stones must be excluded. Malignant etiologies of lower urinary tract pain, such as CIS (carcinoma in situ) or prostate cancer, and common benign options like urolithiasis and sexually transmitted infection (STI) must be excluded.

In the absence of identifiable specific causes, treatment is directed towards symptom amelioration, and phenotypic classification into urinary, psychosocial, organ-specific, infection, neurologic/systemic, and tenderness domains provides direction to any treatment. There remains a paucity of large randomized controlled trials, but multimodal therapy with patients commonly needing an average of three separate treatments has shown promise.

The search for a consistent pathophysiological mechanism continues but remains elusive.

Keywords Male dysuria • Prostate pain • Chronic pelvic pain syndrome (CPPS) • Chronic bacterial prostatitis • UPOINT phenotypic domains

Introduction

The management of men with prostatic-urethral and/or pelvic pain and/or pain on voiding (dysuria) is problematic. It is essential to identify specific causes and exclude an infective or malignant etiology. The identification of urinary tract infection

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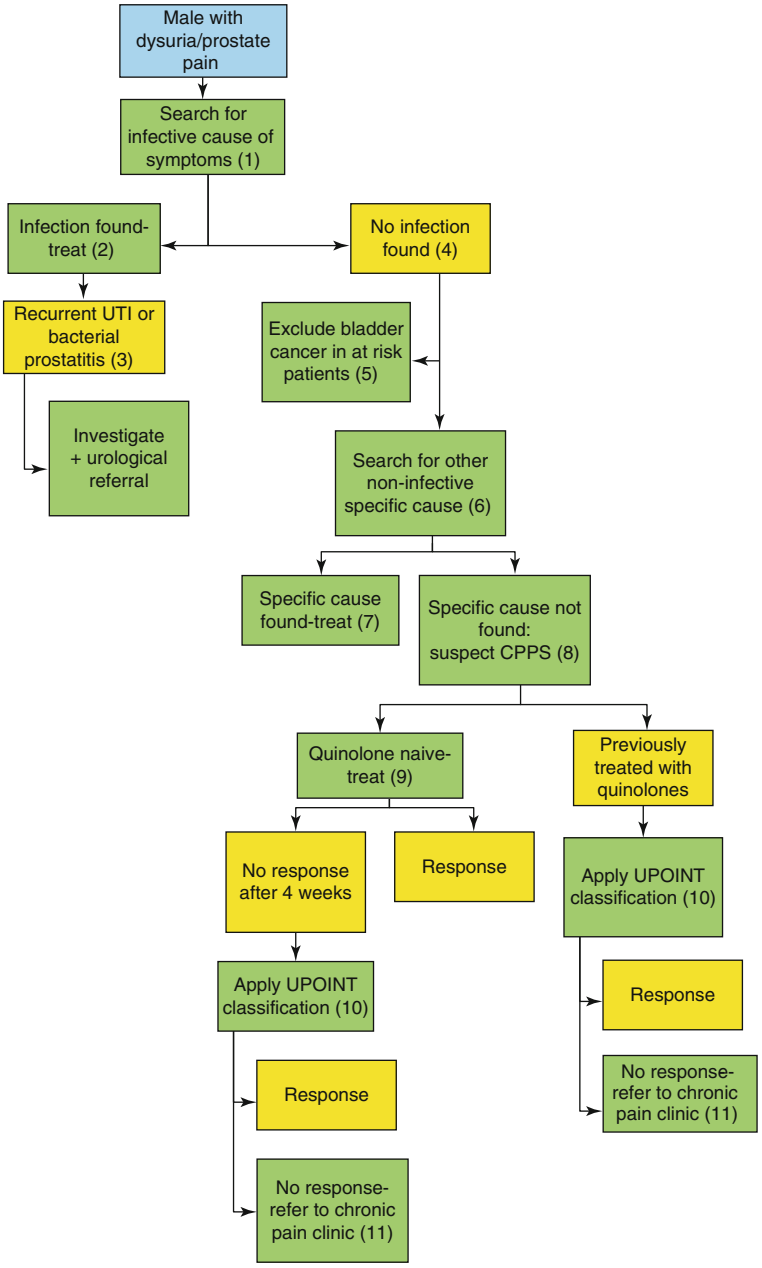
(UTI) needs assessment of the urinary tract for underlying causes. The bulk of men with prostatic pain (approximately 90 %) do not have an identifiable infective etiology and are classified as having chronic pelvic pain syndrome (CPPS).

CPPS remains an enigmatic condition causing frustration amongst patients and clinicians alike. The precise etiology is poorly defined, and the lack of any objective measure or test to confirm the diagnosis or direct a specific therapy results in empirical and haphazard patient management. It is the commonest reason for a man aged less than 50 years to visit a urologist in the USA and has a similar prevalence in Northern Europe.

Presentation and Assessment of Men with Dysuria and/or Prostatic-Urethral Pain

Comments About Flowchart 14.1

1. Symptoms of frequent voiding, pain on voiding, and bladder pain merit urinalysis and if suggestive of UTI, urine culture (MSU) to identify organisms and their sensitivities.
2. If urinalysis and MSU are consistent with an infection, antibiotic treatment should be recommended based on the results of sensitivity. Most of the time, an MSU is unable to identify prostatic bacteria. Culture of prostatic discharge or of urine sample produced after prostatic massage has been proposed as a more sensitive method to detect a prostatic infection (either acute or chronic bacteria prostatitis). If the latter is not feasible, a sperm culture represents an acceptable alternative. When sensitivity tests are not available, empirical treatment with quinolone is an option. Since most of male UTIs are considered complicated, a minimum 7 days duration of treatment is recommended. The presence of fever with shivering is highly suggestive for acute prostatitis, also termed type I prostatitis (Table 14.1). Antibiotic treatment should be started immediately irrespective of the results of MSU (see also Chap. 12).
3. Men with history of recurrent UTI require assessment of prostatic symptoms, flow rate, and residual volume; renal tract ultrasound (USS); and flexible cystoscopy. A urological referral is advisable in such cases. If there is no underlying cause and bladder outlet obstruction is excluded, then chronic bacterial prostatitis (type II prostatitis according to Table 14.1) is most likely the etiology. Prostatic localization studies should be reserved for men with recurrent urinary tract infections (UTIs), to distinguish chronic bacterial prostatitis from other causes of recurrent urinary infections.
4. If no evidence of infection is found, suspicion should be directed to exclude a number of pathologies listed in Table 14.2.
5. Exclusion of urothelial cancer is warranted when there are storage (frequency, urgency, nocturia) lower urinary tract symptoms, particularly if hematuria or risk factors of smoking or exposure to carcinogens are present.



Flowchart 14.1 In office management of male dysuria/prostatic-urethral pain

Table 14.1 Classification of prostatitis (1995) currently in use

Disease	Type of disease
Acute bacterial prostatitis	Type I
Chronic bacterial prostatitis (CP)	Type II
Chronic pelvic pain syndrome (CPPS)	Type III a – inflammatory
	Type III b – noninflammatory
Asymptomatic	Type IV

Table 14.2 Specific pelvic pain causes (other than UTI) that need exclusion before making a diagnosis of chronic prostatitis/chronic pelvic pain syndrome

Sexually transmitted infection (STI)
Prostatic abscess
Prostate cancer
Urolithiasis
Bladder cancer
Gastrointestinal pathology
Musculoskeletal pathology, e.g., PID (prolapsed intervertebral disc)

6. A careful history, examination, and relevant investigations should be performed to exclude any other pathology (Table 14.2). Clinical examination should include palpation of the prostate, perineum, and pelvic floor. Investigation should be directed at identifying a specific cause though in only 10 % of cases will the search be fruitful. The presence of a urethral discharge prompts the clinician to exclude a urethritis by means of urethral swabs. Serum PSA may be performed in those at risk of prostate cancer although levels may be elevated in the presence of inflammation or infection. If directed by symptoms, such as a history suggestive of ureteric colic or bowel pathology, cross-sectional imaging of abdomen and pelvis is warranted. Scrotal ultrasound is recommended in cases of testicular pain but offers little discriminatory value. Normal imaging does, however, provide reassurance and allay the fears of cancer which patients frequently hold.
7. Any disease identified should undergo specific treatment.
8. CPPS is often a diagnosis of exclusion when diseases in Table 14.2 have been excluded. CPPS is a term that comprises all the prostatitis cases where an infective etiology cannot be proven (type III prostatitis according to Table 14.1). Patients with CPPS present with a combination of symptoms of peri-genital pain, often accompanied by urinary and sexual dysfunction, which can greatly impair their quality of life. To meet the diagnostic criteria, these symptoms should have been present for at least 3 months.
9. The evidence for antibiotic usage is weak for CPPS where no organisms have been identified. However, patients that are naive to quinolone therapy may gain some benefit, though this may be as a result of their anti-inflammatory rather than antimicrobial effect. For this reason, a 1-month course of the quinolone ciprofloxacin or levofloxacin is recommended.
10. For those CPPS patients who have failed empirical antibiotic therapy, a number of single agents can be attempted with controversial results. Alpha-blocker

Table 14.3 Clinical phenotypes of the UPOINT domains

Phenotype domains	Clinical features
Urinary	Bothersome lower urinary tract symptoms or high post-micturition residual volume
Psychosocial	Presence of catastrophization or clinical depression
Organ-specific	Prostate tenderness, hemospermia, or leukocytes in prostatic fluid or post-massage urine
Infection	Gram-negative bacilli or Enterococcus localized to prostate or Ureaplasmas in urine
Neurologic/systemic	Pain outside abdomen and pelvis or concurrent diagnosis of fibromyalgia, chronic fatigue, or irritable bowel syndrome
Tenderness	Palpable muscle spasm or trigger points in abdomen or pelvic floor

therapy in CPPS has shown no strong evidence although patients with urinary symptoms are more likely to experience urinary symptomatic improvement. Nonsteroidal anti-inflammatory agents (NSAIDs) may also provide some relief of pain and thereby improve quality of life, but prolonged usage, in view of side effects, is not advised. The phytotherapeutic agents Cernilton and Quercetin have led to an improvement in symptoms. These agents have anti-inflammatory as well as antioxidant properties and, in the case of Cernilton, some alpha-blocker effects. In addition, Quercetin has antibacterial and antifungal properties. The precise action that is responsible for symptom improvement, however, is not known. Neuromodulatory medication has become popular, as in many other chronic pain conditions, though the evidence for its efficacy is weak. Stress reduction and coping strategies may provide benefit whether used alone or in conjunction with formal physiotherapy programs such as the Stanford technique.

It is unlikely that there is one specific cause or pathway contributing to the symptom complex of type III prostatitis or CPPS. In the absence of the identification of a specific etiology, treatment is directed towards amelioration of symptoms and improvement of quality of life. During patient assessment, the most troublesome symptoms and their impact should be defined, in order to develop a clinical phenotype so that treatments can attempt to be more targeted. The UPOINT classification (Table 14.3) has introduced this approach and the concept of multimodal therapies with more encouraging early outcomes than single-agent or sequential treatments. Patients most commonly have three positive domains, with organ-specific, tenderness, and urinary domains being most prevalent. By applying multimodal treatment targeted upon individual UPOINT phenotype of CPPS (as shown in Table 14.4), an 80 % significant improvement in symptoms can be achieved.

11. Failure to respond to the UPOINT management approach should lead to onward referral to a specialized pain clinic in hospital.

Table 14.4 Treatment recommendations for the UPOINT domains

Phenotype domains	Treatment
Urinary	α-blockers, antimuscarinics, e.g., tolterodine or both
Psychosocial	Psychiatric or psychological management of stress or clinical depression, cognitive behavioral therapy, and counseling
Organ specific	Quercetin products without vitamin C, Cernilton (grass pollen extract), finasteride, alpha-blockers, and prostatic massage
Infection	Culture-specific antibiotics or clarithromycin 500 mg BD for 10 days for Ureaplasma-positive patients
Neurologic/systemic	Amitriptyline 10–50 mg OD or pregabalin 75–150 mg BD, or gabapentin 100–300 mg TDS with dose dependent on response
Tenderness	Pelvic floor physical therapy/myofascial release, general physiotherapy, and relaxation exercises. Skeletal muscle relaxants

Conclusion

CPPS is a highly prevalent condition and a treatment challenge both for the general practitioner and the urologist. Many patients present with long histories, poor responses to treatment, and ingrained frustration from the lack of an adequate explanation of symptoms. The blind perseverance with antibiotic therapy in the belief that the condition is caused by infection can only hamper progress in patient management. The UPOINT domains' paradigm of multimodal therapy has shown some short-term promise and currently is the favored approach in chronic pelvic pain syndrome management.

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Chapter 15
Female Dysuria/Urinary Tract Infection

Dario Vigna, Paolo Gontero, and Roberto Carone

Abstract Female dysuria comprises a broad range of urinary symptoms that can be categorized into 2 groups: (1) burning, pain, or other discomfort during micturition and (2) voiding urinary symptoms (hesitancy, slow strain, intermittency, splitting, straining to void, terminal dribble).

Burning sensation during micturition is certainly the most common type of dysuria in the female. Though it is usually supposed to represent bacterial cystitis, this symptom occurs with other well-established causes, both infectious (urethritis, tuberculosis, vulvovaginitis) and noninfectious (e.g., hypoestrogenism, post-radiotherapy cystitis, urogenital neoplasms).

Voiding symptoms are far less common in women than in men, although their incidence may be underestimated. Voiding symptoms do not usually need an urgent urological evaluation, even though in some cases they can lead to severe complications like bladder dysfunction and hydronephrosis; the reason they should never be underestimated.

On the whole, this chapter is structured in three main flowcharts. The first one covers basic investigation and management of burning, pain, or other discomfort during micturition; the second one concerns proper use of antibiotic therapy and prophylactic measures after a diagnosis of lower urinary tract infection. Finally, the

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last flowchart describes basic investigation and management of female voiding symptoms.

Keywords Dysuria • Urinary tract infection (UTI) • Burning • Pain • Urine dipstick • Urine culture • Urine cytology • Antibiotic • Voiding symptoms

Introduction

While the term dysuria literally means "abnormal micturition," it is more often used to describe the burning sensation, characteristic of urinary tract infection (UTI). In this chapter, we have decided to use the term in its wider range of meanings, including any change from normal sensation or function experienced by the woman during the act of micturition. Consequently two different types of definition will be discussed:

1. Dysuria as the complaint of burning or other discomfort during micturition
2. Dysuria as the complaint of voiding symptoms (hesitancy, slow strain, intermittency, splitting, straining to void, terminal dribble)

The first type of dysuria is certainly the most common among females, and it is also the most uncomfortable. Urinary tract infections represent only one of its possible causes; other etiologies will be briefly addressed here. Discomfort may be intrinsic to the lower urinary tract (bladder/urethra) or external (socalled vulvar dysuria).

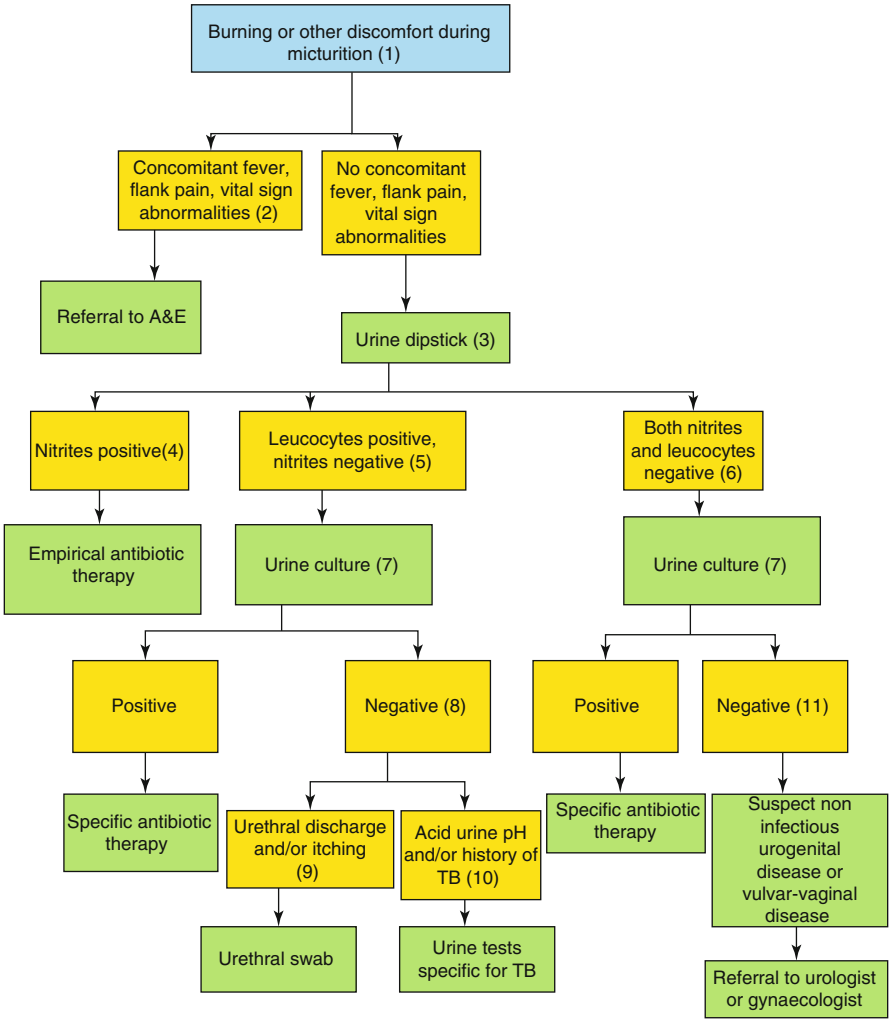
The second type of dysuria is less common but probably underestimated. Voiding symptoms do not usually need an urgent urological evaluation, even though in some cases they can lead to severe complications like bladder dysfunction and hydronephrosis.

The aim of this chapter is to provide a practical algorithm to make a differential diagnosis among the most common etiologies of dysuria in the female and to provide basic information for the work-up of those that can be managed by the GP.

Basic Investigation and Management of Burning and/or Other Discomfort During Micturition in the Female

Comments About Flowchart 15.1

1. The sensation of burning, pain, or other discomfort during micturition in a female patient can be attributed to several infectious and noninfectious etiologies (Table 15.1). The most common cause is a urinary tract infection. This condition can be defined as the microbiological evidence of significant bacteriuria and pyuria, usually accompanied by symptoms such as increased bladder sensation, urgency, frequency, burning during micturition, urgency incontinence, and/or pain in the lower urinary tract (acute cystitis). It has to be emphasized that no sign or symptom on its own is powerful enough to rule in or rule out a diagnosis of UTI;



Flowchart 15.1 Burning and/or other discomfort during micturition in the female

the whole set of symptoms should lead the clinician to get the correct diagnosis. Among signs and symptoms that can be found associated with dysuria, urgency, frequency, and hematuria are the most significant to increase the probability of UTI, while concomitant vaginal discharge and irritation significantly decrease the probability of UTI in the same patient. Other findings, such as lower abdominal pain and costovertebral angle tenderness, are poor predictors of a diagnosis of urinary tract infection. Although physical examination is mostly useless for diagnosing an uncomplicated urinary tract infection, it can reassure the patient

Table 15.1 Causes of burning or other discomfort during micturition in the female

Urinary tract infections (cystitis, pyelonephritis)
Urethritis
Urogenital tuberculosis (TB)
Vulvovaginitis
Hypoestrogenism
Hypersensitivity to products for genital hygiene
Post-radiotherapy cystitis
Urethral diverticula
Urogenital neoplasms (bladder, urethral, or vaginal carcinoma)
Bladder calculi, intravesical foreign bodies
Bladder pain syndrome/interstitial cystitis

and her doctor that other, more serious conditions (pyelonephritis, pelvic inflammatory disease, among others) are unlikely.

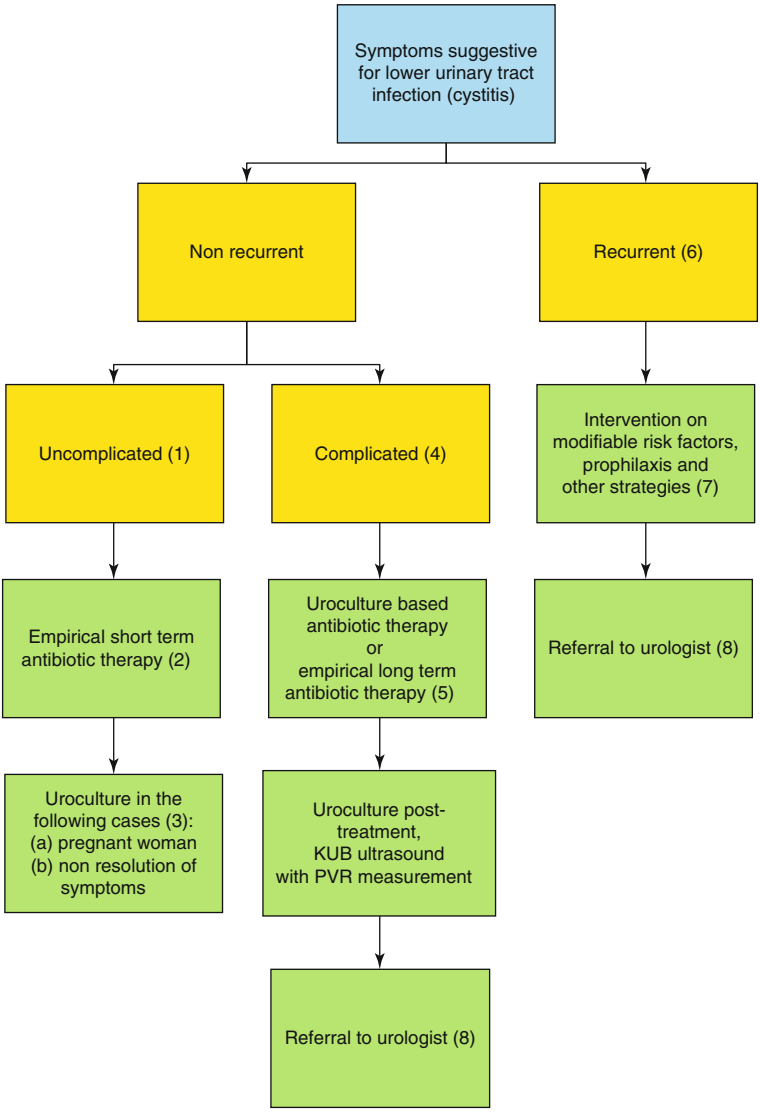
2. Concomitant fever, possibly associated with other symptoms like flank pain, nausea, vomiting, or vital sign abnormalities (tachycardia, tachypnea, hypotension), are consistent with pyelonephritis; in such a situation an urgent referral to an emergency department is needed (see Chap. 12,Table 12.2).
3. The mainstay for the diagnosis of UTI is urine culture, allowing a clear demonstration of bacteria involved in pathogenesis of the patient's infection and the consequent choice of a specific antibiotic therapy. Nevertheless, urinaryculture is a time-consuming test. Dipstick testing for nitrites and leukocytes is usually recommended in general practice for a fast assessment of fresh urine in uncomplicated symptomatic patients.
4. If nitrites (with or without leukocytes) are positive, the patient is very likely to have a urinary tract infection, and empirical antibiotic treatment (see Flowchart 15.2) is justified.
5. If leukocytes (but not nitrites) are positive, only half of patients will have an infection.
6. If both nitrites and leukocytes are negative, most patients will not have any infection and antibiotics should not be given.
7. When urine dipstick shows leukocytes only or is negative for both leukocytes and nitrites, antibiotic therapy should be delayed until results of urine culture are known.
8. In the case of a positive dipstick for leukocytes and a negative urine culture, two diagnosis need to be ruled out: urethritis and genitourinary tuberculosis.
9. Urethritis is a typical sexually transmitted disease, attributable to Chlamydia trachomatis, Neisseria gonorrhoeae, or herpes simplex virus. Its clinical presentation is similar to acute cystitis but with milder symptoms and a less quick onset. Discharge at the urethral meatus is an inconsistent finding, while quite a common symptom is urethral burning or itching even outside of micturition. Dipstick test is usually positive for leukocytes and pyuria, but urine culture is negative. In this case a urethral swab should be taken to confirm the clinical diagnosis.

10. Genitourinary tuberculosis is a diagnosis which should be suspected in patients whose clinical history includes prior pulmonary tuberculosis or who are at risk from having from tuberculosis. This is particularly true exposure when urine analysis is characterized by acid pH and no benefit has been experienced from previous antibiotic therapies. Diagnosis is usually confirmed by microscopic examination of urinary sediment by Ziehl-Neelsen stain or with a urine culture by the Lowenstein-Jensen medium; the latter method is the most time-consuming (about 2 weeks) but also the accurate in terms of sensibility and specificity.
11. In the case of a negative dipstick and a negative urine culture, a urinary tract infection can be excluded and other causes of dysuria should be considered, first of all vulvovaginitis (vulvar dysuria). Vaginitis is an inflammatory condition attributable to Candida or Trichomonas species, which can be suspected in cases of vulvar itching, dyspareunia, and a smelly vaginal discharge. Dipstick test is negative for pyuria and bacteriuria, provided collection of the urine has been properly done. Other possible causes of dysuria associated with negative urine analysis and urine culture are noninfectious entities such as hypoestrogenism, hypersensitivity to products for genital hygiene, post-radiotherapy cystitis, urogenital neoplasms, urethral diverticula, bladder calculi or endovesical foreign bodies, and bladder pain syndrome/interstitial cystitis (BPS/IC). Urine cytology and bladder ultrasonography are mandatory to rule out bladder cancer. Referral to a urologist or a gynaecologist is advisable.

Comments About Flowchart 15.2

1. A lower urinary tract infection (cystitis) that is uncomplicated (i.e. without the risk factors listed in Table 15.2) can be easily managed by the general practitioner without the need for a urological consultation.
2. Several agents can be used effectively as single-dose or short-course regimens without the need for the results of urine cultures. First-line options include a single 3 g oral dose of fosfomycin trometamol, a 3-day course of pivmecillinam 400 mg BID, or a 5–7-day course of nitrofurantoin 100 mg BID. Cotrimoxazole 160/800 mg BID for 3 days or trimethoprim 200 mg BID for 5 days should only be considered as drugs of first choice in areas with known resistance rates for *E. coli* < 20 %.

 Fluoroquinolones have been shown to exhibit comparable efficacy to cotrimoxazole for uncomplicated cystitis, but given their value in the treatment of pyelonephritis and complicated UTI, fluoroquinolones should best be used as second-line therapy. Amoxicillin-clavulanate cannot be recommended either as first- or second-line option unless no other alternatives are available, or the patient is a pregnant woman; in the latter case penicillin and cephalosporin are the only safe antibiotics both for the mother and the fetus, duration of 3 days is recommended.
3. In order to ascertain the complete eradication of microorganisms after clinical resolution of an episode of uncomplicated UTI, routine urine culture is only indicated in pregnant women, as it has been demonstrated that asymptomatic bacteriuria in pregnancy is an important risk factor for pyelonephritis and premature delivery. Urine



Flowchart 15.2 Management of lower urinary tract infection in females

culture is also necessary in non-pregnant woman symptoms persist after antibiotics. A positive urine culture warrants a specific antibiotic therapy based on the results of the culture. In this case a 7-day regimen should be considered.

4. A complicated lower UTI is any urinary infection occurring in patients with an underlying predisposing condition, whether medical, functional, or anatomical, which increases the risk for infection and recurrence, reduces the effectiveness of therapy, or shifts the spectrum of the causative microorganisms toward

Table 15.2 Risk factors for complicated UTI

Indwelling catheter or intermittent catheterization
Increased post-void residual urine
Obstructive uropathy of any etiology (including neurogenic urinary bladder)
Vesicoureteric reflux
Urinary tract modifications (e.g., an ileal neobladder)
Renal insufficiency, diabetes mellitus, immunodeficiency

antimicrobial-resistant strains. Risk factors that render a UTI complicated are shown in Table 15.2.

5. In these patients urinary infection should be ideally treated based on the results of urine cultures. Alternatively, an empirical therapy, with broader-spectrum antibiotics (fluoroquinolones, third-generation cephalosporins, aminoglycosides) extended for up to 10–14 days should be considered.
6. A recurrent UTI is defined as the occurrence of at least three episodes of uncomplicated UTI in the last 12 months, with at least one documented by urine culture. Risk factors vary depending on women's hormonal status:

 (a) In premenopausal women:

 - Previous episodes of cystitis
 - Frequent or recent sexual activity
 - Use of spermicidal agents
 - Maternal history of cystitis
 - Cystitis at an early age

 (b) In postmenopausal women:

 - Diabetes mellitus
 - Urinary incontinence
 - History of UTI before menopause
 - ABO blood-group antigen non-secretor status

7. Several strategies can be followed to prevent recurrent UTIs:

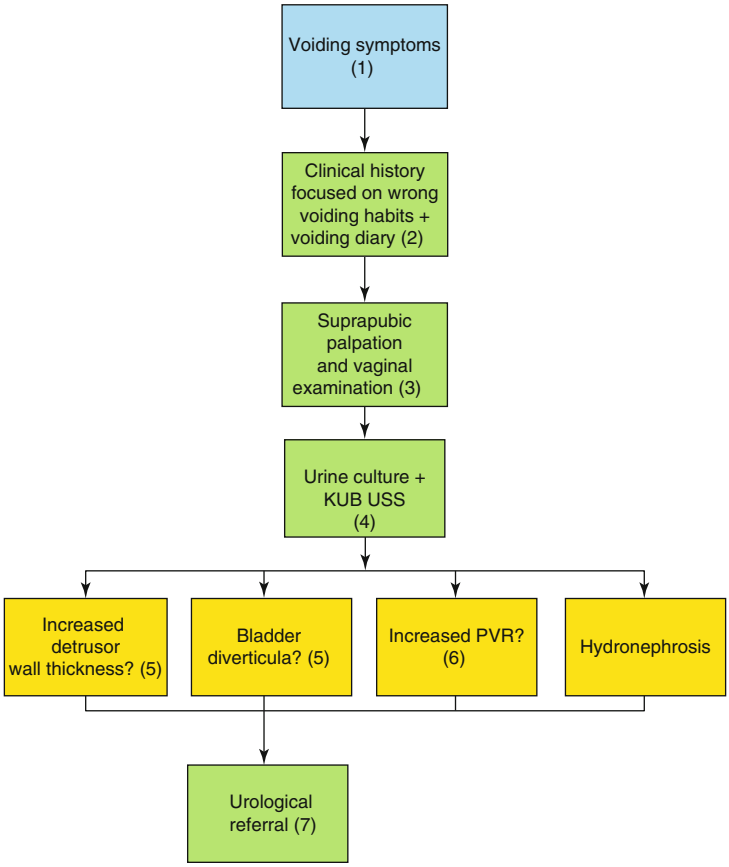
 - Intervention on modifiable risk factors (i.e., abolishing the use of spermicidal agents, optimizing glycemic control, improving the treatment of urinary incontinence)
 - Antimicrobial prophylaxis with a reduced dose, either continuously or after sexual intercourse
 - Patient-initiated treatment of every recurrent episode at an early stage
 - Unspecific prophylaxis with cranberry extracts
 - Local hormonal treatment in postmenopausal women

8. A urological referral is recommended either in case of complicated UTI or recurrent UTI, particularly when multiple prophylactic or treatment strategies have failed.

Management of Voiding Symptoms in the Female

Comments About Flowchart 15.3

1. Voiding symptoms represent an entirely different type of dysuria. Patients typically report a slow urine stream, without associated pain or burning sensation. There is often a history of abdominal straining to initiate, maintain, or improve the urinary stream. Voiding dysfunction can involve a detrusor hypocontractility or a urethral obstruction. A correct pathophysiological diagnosis can be provided only by relatively invasive investigations such us urodynamics, although the majority of women who report voiding symptoms eventually will not undergo such complex investigations.
2. The first step is to identity an incorrect voiding habit, usually characterized by an excessively protracted interval between two consecutive micturitions (more than 4 h). This is the most important modifiable risk factor, which predisposes to detrusor damage due to chronic overdistension of the bladder. For this purpose a 3-day voiding diary is a simple but useful tool; it allows the clinician to objectively assess patient's urinary frequency and voided volumes, each of which should not exceed 300–350 ml.
3. Physical examination should rule out a significant pelvic organ prolapse, (a potential cause of infravesical obstruction), and a suprapubic abdominal distension, secondary to chronic urinary retention.
4. It is advisable to ask for urinalysis and culture in order to rule out a UTI. A kidney and bladder ultrasound study (KUB USS) can provide useful information about the patient's bladder (detrusor wall thickness, bladder diverticula, post-void residual urine) and kidneys (presence or absence of hydronephrosis).
5. Similarly to the male counterpart, increased detrusor wall thickness and bladder diverticula suggest, a urethral obstruction.
6. There are no well-defined cutoff values for post-void residual (PVR) of urine, although most of the experts believe that a PVR > 100 ml must be considered pathological. Moreover, it is believed that increased PVR is an index of bladder contractility rather than of urethral obstruction.
7. A subsequent urological consultation may include a urodynamic study guiding the most appropriate treatment (pelvic floor rehabilitation, intermittent self-catheterization, sacral neuromodulation, surgery for pelvic organ prolapse).



Flowchart 15.3 Management of voiding symptoms in females

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Chapter 16
Oliguria

Robin G. Woolfson

Abstract Oliguria is most commonly due to hypovolemia leading to renal hypoperfusion. If uncorrected, it may lead to significant acute kidney injury. This chapter provides a guide to the assessment, investigation, and management of the oliguric patient.

Keywords Oliguria • Acute kidney injury

Introduction

Oliguria means low urine output and is defined as an output of less than 1 mL/kg/h in infants and less than 0.5 mL/kg/h in children and adults. Oliguria frequently occurs in acute kidney injury (AKI), and most commonly, it reflects hypovolemia and reduced renal perfusion although other causes include intrinsic renal disease and postrenal or obstructive nephropathy (Table 16.1).

Two thirds of community-acquired AKI is due to hypovolemia with sepsis, surgery, heart failure, and drugs implicated in episodes affecting inpatients. Rapid correction of reversible causes may prevent the development of intrinsic renal disease with its associated comorbidities and the risk of mortality which may be as high as 50 %. A careful history and clinical examination with particular focus on volume status will often identify the cause of oliguria, particularly if the cause is prerenal or postrenal where early diagnosis and treatment may result in complete recovery. AKI is not always associated with oliguria, and nonoliguric AKI usually reflects a less severe renal injury with a better prognosis.

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Table 16.1 Causes of oliguria and acute kidney injury

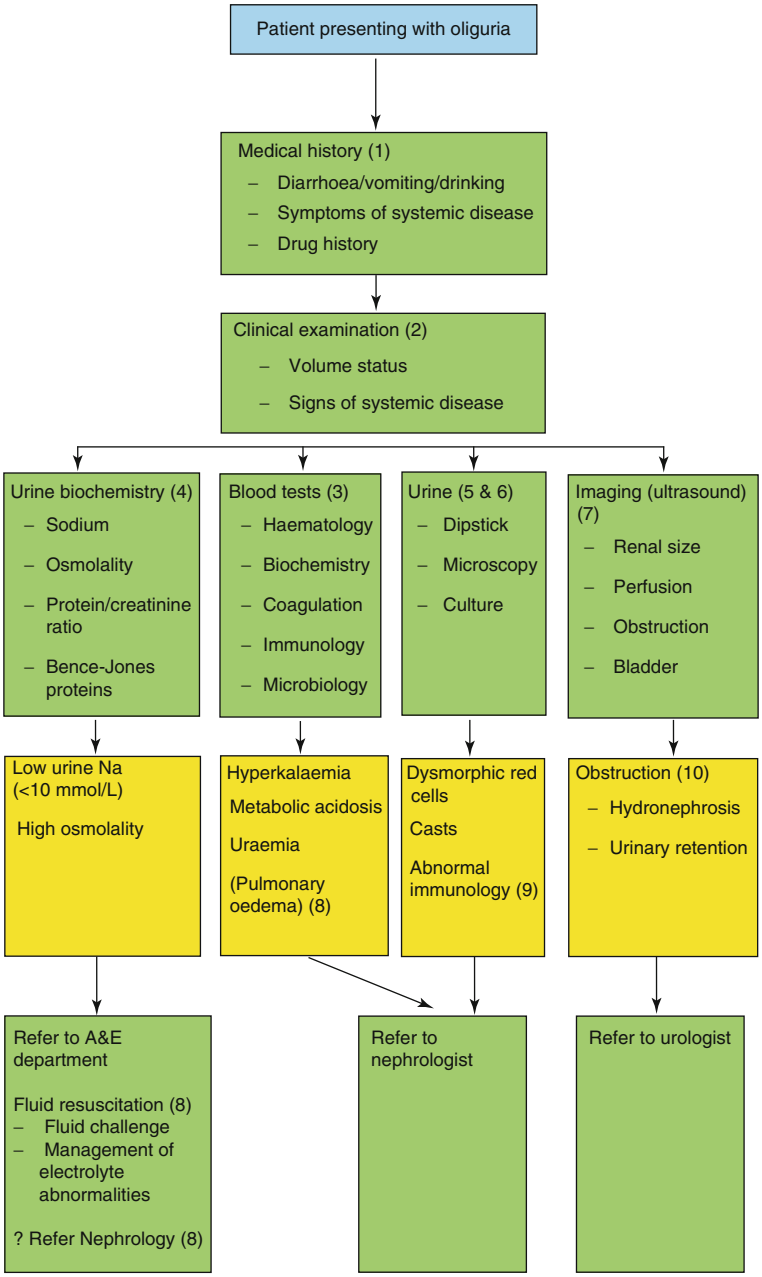
Site of origin of oliguria	Type of mechanism	Result	Etiology
Prerenal/renal hypoperfusion	Circulating hypovolemia	Fluid loss	Inadequate fluid intake
			Diarrhea
			Vomiting
			Fever
			Hemorrhage
			Burns
		Fluid in the wrong compartment	Pancreatitis
			Ascites including hepatic failure
			Nephrotic syndrome
	Pump failure	Cardiac failure	
		Massive pulmonary embolus	
	Circulation failure	Septicemia/severe infection	
		Hepatorenal syndrome	
Renal/intrinsic disease	Prolonged hypoperfusion	Renal ischemia	All causes of hypovolemia
			Renal artery clamping during kidney surgery
			Renal infarction
	Toxic	Drugs	e.g., NSAIDs
		Poisons	
		Radiocontrast	Contrasts for IVP, CT, and MRI
		Pigmenturia	Hemolysis
			Rhabdomyolysis
	Immunological	Glomerulonephritis	Vasculitis
			Lupus
			Goodpasture's
			Postinfectious GN
		Interstitial nephritis	Drugs
			Autoimmune disease
	Vascular	Macrovascular	Aortic dissection/renal artery occlusion
			Renal vein thrombosis
		Microvascular	Hemolytic-uremic syndrome
			Malignant hypertension
			Preeclampsia
			Scleroderma renal crisis
Postrenal	Upper urinary tract obstruction	Hydronephrosis	Ureteric tumors
			Retroperitoneal fibrosis
			Ureteric calculi
			Bladder cancer
			Prostate cancer
	Lower urinary tract obstruction	Retention of urine	Benign prostatic hyperplasia
			Prostate cancer
			Urethral stricture

The aim of this chapter is to provide a practical algorithm to guide a differential diagnosis among the most common etiologies of oliguria and to provide basic information for the work-up of such patients in primary through secondary care.

Investigation and Management of Oliguria

Comments About Flowchart 16.1

1. History
 Establish the duration and symptoms of illness with a detailed previous medical history and drug history (including analgesics, over-the-counter products, and alternative therapies). Ask about dyspnea, anorexia, failure to drink, diarrhea, and vomiting; identify symptoms to suggest systemic disease, including rash, arthralgia, myalgia, painful red eyes, recurrent oral ulceration, Raynaud's phenomenon, dyspnea, hemoptysis, bone pain and recent fractures, weight loss, and fever. Ask about lower urinary tract symptoms, particularly reduced urine flow and hematuria.
2. Clinical examination
 (a) Volume assessment: Tachycardia, orthostatic hypotension, reduced jugular venous pressure, reduced skin turgor, cold extremities, and slow peripheral capillary refill suggest hypovolemia. Edema, pulmonary edema, presence of cardiac murmurs, and added heart sounds may suggest fluid overload.
 (b) General examination: rash, cutaneous vasculitis, lymphadenopathy, chest examination for evidence of infection or pulmonary edema, abdominal examination for palpable kidneys, and palpable bladder.
3. The following blood tests should be requested: full blood count; biochemistry; clotting screen; creatine kinase; serum immunoglobulins and protein electrophoresis; complement levels; PSA; autoantibodies including antinuclear antibody (ANA), double-stranded deoxyribonucleic acid (dsDNA), extractable nuclear antigen (ENA), anti-glomerular basement membrane antibody (anti-GBM), anti-neutrophil cytoplasmic antibody (ANCA), rheumatoid factor, and antistreptolysin O Titer (ASOT); viral serology; and blood cultures.
4. Urine biochemistry: Low urine sodium and increased osmolality are found in patients with oliguria (unless there is recent diuretic administration) due to renal hypoperfusion who have physiological oliguria (avid salt and water retention). Send urine for protein/creatinine ratio and Bence-Jones proteins.
5. Urine dipstick: Look for hematuria, free hemoglobin or myoglobin, proteinuria (but not Bence-Jones protein), or glycosuria.
6. Urine microscopy: to confirm red cells if present and differentiate from free hemoglobinuria or myoglobinuria. Identify tubular casts which may suggest parenchymal disease. Urine culture to identify infection.
7. Imaging: ultrasound of kidneys and bladder to measure renal size and cortical echogenicity and exclude obstruction. Doppler signal to confirm renal perfusion. Chest x-ray.



Flowchart 16.1 Management of patient presenting with oliguria

8. Prerenal: fluid resuscitation using salt-based solution.
 (a) Ensure adequate venous access.
 (b) Fluid challenge with 250 ml colloid or normal saline over 5 min looking for signs of clinical improvement with rise in jugular venous pressure or central venous pressure (if monitored). Repeat fluid challenges at 5–15 min intervals until rise in JVP or CVP is sustained.
 (c) Monitor electrolytes (Na, K, chloride, bicarbonate, calcium) and treat abnormal levels as required.
 (d) Refer nephrology team if biochemistry is very abnormal. Dialysis may be required if with severe hyperkalemia, severe metabolic acidosis, fluid overload with pulmonary edema, or severe uremia.
9. Intrinsic renal disease: Refer to nephrology team for further investigations including renal biopsy.
10. Postrenal: referral to urology team for decompression of urinary tract with bladder catheter (urethral or suprapubic) or percutaneous nephrostomy depending on level of obstruction.
 (a) Ensure adequate venous access for fluids and intravenous antibiotics if there is possibility of urinary infection.
 (b) If biochemistry is abnormal, then post-obstructive diuresis is likely, so prepare intravenous saline. Maintain accurate record of fluid balance.
 (c) Referral to nephrology team if biochemistry is very abnormal.

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Chapter 17
Erectile Dysfunction

Culley C. Carson III

Abstract Erectile dysfunction (ED) afflicts more than 50 % of men over 40 years of age. Its causes are often linked to vascular disease, and ED may be the first symptom of vascular disease often preceding an acute vascular event by 3–5 years. ED can also be associated with radical pelvic surgery, diabetes, testosterone deficiency, neurological disorders, and depression. Lifestyle associations include obesity, sleep apnea, tobacco use and drug abuse.

Evaluation for ED includes use of standard questionnaires such as the Sexual Health Inventory for Men (SHIM), a careful history, and a physical examination focused on the genitourinary system. Laboratory studies should include glucose, lipid profile, and serum testosterone.

Treatment of ED should begin with lifestyle modification such as diet, exercise, and smoking cessation. The treatment of ED has been enhanced by the introduction of the phosphodiesterase type 5 inhibitors (PDE5i). These drugs have a success rate of greater than 70 % with an excellent safety profile. PDE5i drugs should be taken 1 h before sexual stimulation and have a half-life of 4–17 h. These agents' efficacy is enhanced by normalizing testosterone in hypogonadal men.

Should PDE5i drugs fail, second-line treatment can be considered. These options include vacuum erection device, pharmacoactive agents injected into the corpora cavernosa, and urethral prostaglandin suppositories. Surgical implantation of a penile prosthesis provides excellent function for men who fail less invasive alternatives or who desire a surgical solution to their ED.

Keywords Impotence • Erectile dysfunction • Hypogonadism • PDE5 inhibitors • Erection • Sexual dysfunction

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Introduction

Erectile dysfunction (ED) is the inability to achieve and/or maintain an erection adequate for sexual intercourse. Data from the Massachusetts Male Aging Study show that ED affects some 20–30 million American men, most of whom are older than 50. This epidemiologic study of a homogeneous suburban Boston community surveyed 1,709 men and reports 52 % of men aged 40–70 had erectile dysfunction: 10 % had complete ED, 25 % moderate, and 17 % minimal. The prevalence of ED increases with age, with moderate and complete ED increasing most markedly. The risks of ED increase substantially in men with cardiac disease, antihypertensive and vasoactive drug use, obesity, and tobacco use.

ED has both organic and psychogenic etiologies with 60 % of patients having organic ED caused by vasculogenic, neurogenic, hormonal, or smooth muscle abnormalities. Fewer than 40 % of patients have pure psychogenic ED.

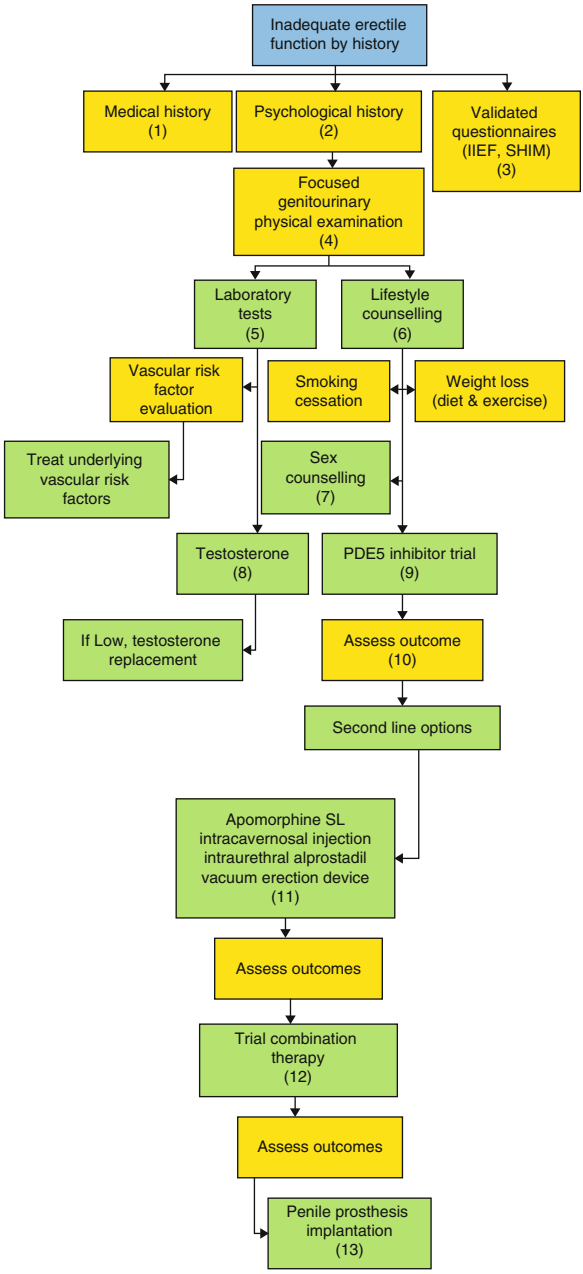
Risk factors for ED include systemic diseases that produce vascular abnormalities, including hyperlipidemia, diabetes mellitus, the results of hypertension and antihypertensive therapy, and atherosclerosis. Neurogenic erectile dysfunction is seen with multiple sclerosis, diabetes mellitus, paraplegia, and following radical pelvic surgery or radiation for pelvic malignancy such as prostate, colon, or bladder cancer. Hormonal abnormalities and hypogonadism are also risk factors for ED, producing not only central nervous system abnormalities and low libido but also local changes in corpus cavernosum smooth muscle relaxation. Psychologic causes are significant, and ED is frequently associated with depression, even of mild degree. Treatment for depression using SSRI medication further enhances ED by decreasing and delaying ejaculatory function.

Management of Erectile Dysfunction

Comments About Flowchart 17.1

1. A careful general and sexual history is the cornerstone in the evaluation and treatment of patients with erectile dysfunction. History should include information regarding age of onset, associated lifestyle changes at onset, speed of onset, and the presence or absence of erections with other partners, during masturbation, and at night and in the early AM. Patients should be asked about ejaculatory function, post-ejaculatory pain, and ejaculatory volume. Careful questioning regarding decreased libido may suggest a hormonal cause but more often is associated with clinical depression. Because ED is highly associated with lower urinary tract symptoms, patients should be asked about voiding symptoms.

 Patients who present with organic ED most often have a gradual onset beginning with intermittent loss of erections, decreased duration, and difficulty with maintaining erections until ejaculation. History is the most proficient method of



Flowchart 17.1 Management of erectile dysfunction

identifying patients complaining of premature ejaculation who may also present for evaluation of ED.

2. Psychogenic ED most often begins with abrupt onset precipitated by psychologic abnormalities such as depression, anxiety disorder, changes in lifestyle, or relationship problems. These men usually have preserved nocturnal and morning erections and may be functional with masturbation. Patients with organic ED also have secondary psychologic ED. Patients with pure loss of libido or with other symptoms of androgen deficiency of the aging male can be identified by a hormone profile.
3. The International Index of Erectile Function is a long instrument used primarily in research. The Sexual Health Inventory for Men (SHIM) is a better tool for clinical evaluation. It has 5 questions and is clinically validated.
4. The physical examination is focused on secondary sex characteristics, hair distribution, and genitalia. Evaluation of peripheral pulses, neurologic reflexes such as the bulbocavernosus reflex, and anal sphincter tone may help to identify some patients with peripheral neuropathy from nerve injury or diabetes. A prostate examination is important to rule out prostatitis. Changes in testicular size and consistency may be associated with primary hypogonadism. General physical examination of blood pressure, lower extremity reflexes and pulses, and visual fields (to evaluate pituitary tumors) may suggest underlying systemic causes for erectile dysfunction.
5. A hormone profile should include a morning total testosterone. If the total testosterone is abnormal, a follow-up repeat total testosterone, free testosterone, LH, and prolactin may identify patients with androgen deficiency, pituitary tumors, or other causes of hypogonadism. Testosterone is typically low and prolactin high in patients who have pituitary tumors or chronic renal failure on hemodialysis. A lipid profile, hemoglobin A1C, and other general medical studies may be helpful.

 For patients requiring additional investigation prior to surgical reconstruction or vascular bypass, specialized investigation such as Doppler penile blood flow studies following injection of vasoactive agents, nocturnal penile tumescence monitoring studies, and pelvic angiography may be helpful. Candidates for vascular bypass are usually young men with solitary pelvic artery lesions and a strong history of perineal or pelvic trauma. Vascular bypass surgery in older patients is rarely successful, especially if ED is associated with hypercholesterolemia, diabetes, hypertension, or smoking. Nocturnal penile tumescence monitoring studies may be helpful in differentiating organic and psychogenic ED in some patients.
6. Initial treatment should focus on modifying medication and lifestyle abnormalities. Smoking cessation and managing diabetes, hypercholesterolemia, and hypertension may improve erectile function and facilitate medical treatment. Modifying antihypertensive medications to include erection-hospitable agents such as alpha-blockers, ace inhibitors, and calcium channel blockers may maintain antihypertensive therapy with restoration of erectile function.
7. If depression or relationship issues are a significant problem, sexual counseling may be helpful in addition to pharmacologic treatment. Office counseling with patient and partner may facilitate understanding of the probable causes of erectile dysfunction, treatment alternatives, and expectations.

8. In patients with hypogonadism, testosterone replacement is necessary to enhance libido and facilitate PDE5i response. Testosterone replacement therapy is by long-acting injectable agents, such as testosterone enanthate or cypionate 200 mg every 2 weeks and topical testosterone gel. The goal of testosterone replacement therapy is to restore testosterone levels to the normal range. The use of testosterone in eugonadal men with psychogenic erectile dysfunction, while raising testosterone beyond normal levels, is both ineffective and associated with significant potential complications. Patients treated with testosterone supplementation should be regularly evaluated with digital rectal examination, PSA, lipid profile, and hematocrit. In younger men concerned about fertility, treatment with clomiphene citrate is a better choice as the effect on sperm count is facilitatory.
9. Oral agents such as sildenafil, tadalafil, vardenafil, and avanafil are first-line treatment of ED. These selective phosphodiesterase type 5 inhibitors (PDE5i) facilitate cGMP concentration, duration, and subsequent corpus cavernosal smooth muscle relaxation. There is improvement in erectile function 30–60 min following PDE5i administration. Most men respond best to 100 mg of sildenafil or 20 mg tadalafil or vardenafil. As many as 8 trials may be required for full success and effectiveness. Side effects include headache, dyspepsia, facial flushing, myalgias, and blue vision. PDE5i have been reported to be significantly better in producing erections than placebo in patients with diabetes mellitus, spinal cord injury, hypercholesterolemia, depression, cardiac disease, following radical prostatectomy, and in psychogenic erectile dysfunction. While PDE5i are effective in virtually all etiologies and severities of ED, they are least effective in patients with severe vascular disease. PDE5i are generally extremely safe drugs; however, they do have additive affects with nitrate agents used for coronary artery disease, producing severe transient hypotension. The use of sildenafil with nitrate drugs is contraindicated. In patients taking sildenafil following radical prostatectomy, results are best after a bilateral nerve-sparing radical prostatectomy.
10. It is critical to assess the outcomes of treatment to select patients for additional treatment options. Coaching patients about the proper dosing and use of PDE5i can rescue many men that do not respond initially.
11. Additional therapeutic alternatives are available if oral agents fail. Intracavernosal pharmacotherapy is effective in producing functional erections. Options include prostaglandin E1 (PGE1) or a combination of papaverine and phentolamine. Initial dose of PGE1 varies from 2.5 to 5 mcg. After an initial in-office titration to a dose that produces a firm erection satisfactory for sexual intercourse that lasts no longer than 60 min, patients are instructed to use the trial dose at home and may titrate higher with physician guidance. If erections last more than 4 h, patients must go to the emergency room for treatment using an alpha-agonist such as intracavernosal phenylephrine. If intracavernosal PGE1 is ineffective or produces excessive pain, a combination of papaverine with or without phentolamine and PGE1 may produce satisfactory erectile function with less penile discomfort. Side effects from this combination include prolonged erections and priapism, corpus cavernosum fibrosis, and occasional transient hypotension.

Transurethral PGE1 is available in 250, 500, or 1,000 mcg pellets. Its effectiveness is approximately 30 %. A small applicator with a pellet of prostaglandin E1 is placed in the urethra. After the pellet is deposited and the applicator removed, the patient stimulates the urethra to allow PGE1 to enter the corpus cavernosum. Erection usually occurs in 10–15 min and is maintained for as long as 40 min. Side effects include prolonged erection and penile pain, aching, or urethral burning.

Vacuum erection devices (VED) have been used to stimulate, facilitate, and prolong duration of erections. These external devices create a vacuum around the penis to produce engorgement and tumescence, maintained by a constrictive ring placed at the base of the penis. While the erections are less natural, they are satisfactory for vaginal penetration and sexual intercourse. The constriction devices may produce penile pain, bruising, scarring, Peyronie's disease and inhibit ejaculations.

12. In men who fail these options, combination of PDE5i and intracavernosal PGE1 has been successful in select patients. This treatment is expensive and only effective in selected patients.
13. Implantation of penile prostheses is a successful method for restoring erectile function in severe ED. These surgically implanted devices are usually inflatable and consist of two hollow cylinders placed in the corpora cavernosa of the penis and connected to a small pump device placed in the scrotum. Normal saline is stored in a reservoir placed beneath the rectus muscles. Patients can compress the pump in the scrotum, fill the cylinders of the corpora cavernosa, and maintain an erection of normal sensation and rigidity throughout sexual intercourse. The device can then be deflated for concealment with excellent cosmetic results. 93 % of devices are functional at 3 years, 86 % at 5 years, and 76 % at 10 years after implantation. Mechanical malfunction is treated with device replacement. Patient and partner satisfaction has been reported in excess of 90 %.

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Chapter 18
Male Factor Infertility

Culley C. Carson III

Abstract Of the 10–20 % of infertile couples, 20 % are purely male factor and 30 % are combined male and female factors. Risk factors include trauma or torsion of the testes, erectile dysfunction, low testosterone, varicocele, and exposure to toxins including chemotherapy, tobacco, and alcohol abuse. Couples should be evaluated after 9–12 months if unprotected intercourse has failed to result in conception.

Evaluation includes two semen analyses each after 72 h of abstention from ejaculation. Semen parameters evaluated include volume, sperm count, motility, and agglutination. Additional studies should include serum testosterone, FSH and LH, and prolactin if testosterone is low. Special studies may include transrectal ultrasound to identify ejaculatory duct obstruction. In special instances, testicular biopsy and vasography may be indicated. All patients should have a basic physical examination to include genital examination with special attention to the testes and penis. A rectal examination to assess the prostate is also important.

Treatment options include hormonal replacement in patients with deficient testosterone. Exogenous testosterone alone may reduce the sperm count. Clomiphene 25–50 mg/day for 6 months may be helpful. For men with a diagnosed varicocele, varicocelectomy may be helpful. For men with ductal obstruction, microsurgical repair may result in improved sperm quality. Ejaculatory dysfunction may be treated medically, or sperm retrieval with artificial insemination may be necessary for severe retrograde ejaculation that does not respond to medication. Retrieval of sperm through vibratory stimulation may also be useful for assisted reproductive techniques (ART).

In refractory patients, donor insemination or advanced ART may be necessary.

Keywords Infertility • Male factor infertility • Varicocele • Hypogonadism • Azoospermia • Assisted reproductive techniques

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Introduction

Infertility affects from 12 to 15 % of couples attempting to conceive. Male factor infertility alone accounts for 20 % of these cases and is a contributor in 30 % of infertile couples. The World Health Organization defines infertility as the "inability of a sexually active non contracepting couple to achieve pregnancy in one year." Couples with infertility usually present to a gynecologist or urologist but may be first evaluated by primary care practitioners. Guidelines for the evaluation and treatment of men with male factor infertility have been recently published by the American Urological Association (AUA) and the European Association of Urology (EAU). These consensus guidelines are evidence based and represent the findings and opinions of urologists who specialize in the treatment of the infertile male.

The evaluation of these patients begins with a history including a sexual history, family history, and general medical history. A focused genitourinary physical examination is followed by semen analyses. Two semen analyses should be evaluated after 72 h of abstention from ejaculation. Standard measurements of semen parameters are listed in Table 18.1 with comparison of previous standards. A hormone profile with testosterone, FSH, LH, and prolactin is important for both evaluation and future treatment. Men with bilaterally absent vasa should be offered, along with their partners, genetic testing for risk factors for cystic fibrosis.

Treatment of male factor infertility may be medical or surgical or involve assisted reproductive techniques (ART) such as ICSI and artificial insemination.

Table 18.1 Comparative standard semen parameters provided by the World Health Organization (WHO)

Semen characteristics	WHO 1980	WHO 1987	WHO 1992	WHO 1999	WHO 2010
Volume (mL)	ND	≥2	≥2	≥2	1.5
Sperm count (10^6/mL)	20–200	≥20	≥20	≥20	15
Total sperm count (10^6)	ND	≥40	≥40	≥40	39
Total motility (% motile)	≥60	≥50	≥50	≥50	40
Progressive motility[a] (%)	≥2[b]	≥25	≥25 (grade a)	≥25 % (grade a)	32 (grade a + b)
Vitality (% alive)	ND	≥50	≥75	≥75	58
Morphology (% normal forms)	80.5	≥50	≥30[c]	14[d]	4[e]
Leukocyte count (10^6/mL)	<4.7	<1.0	<1.0	<1.0	<1.0

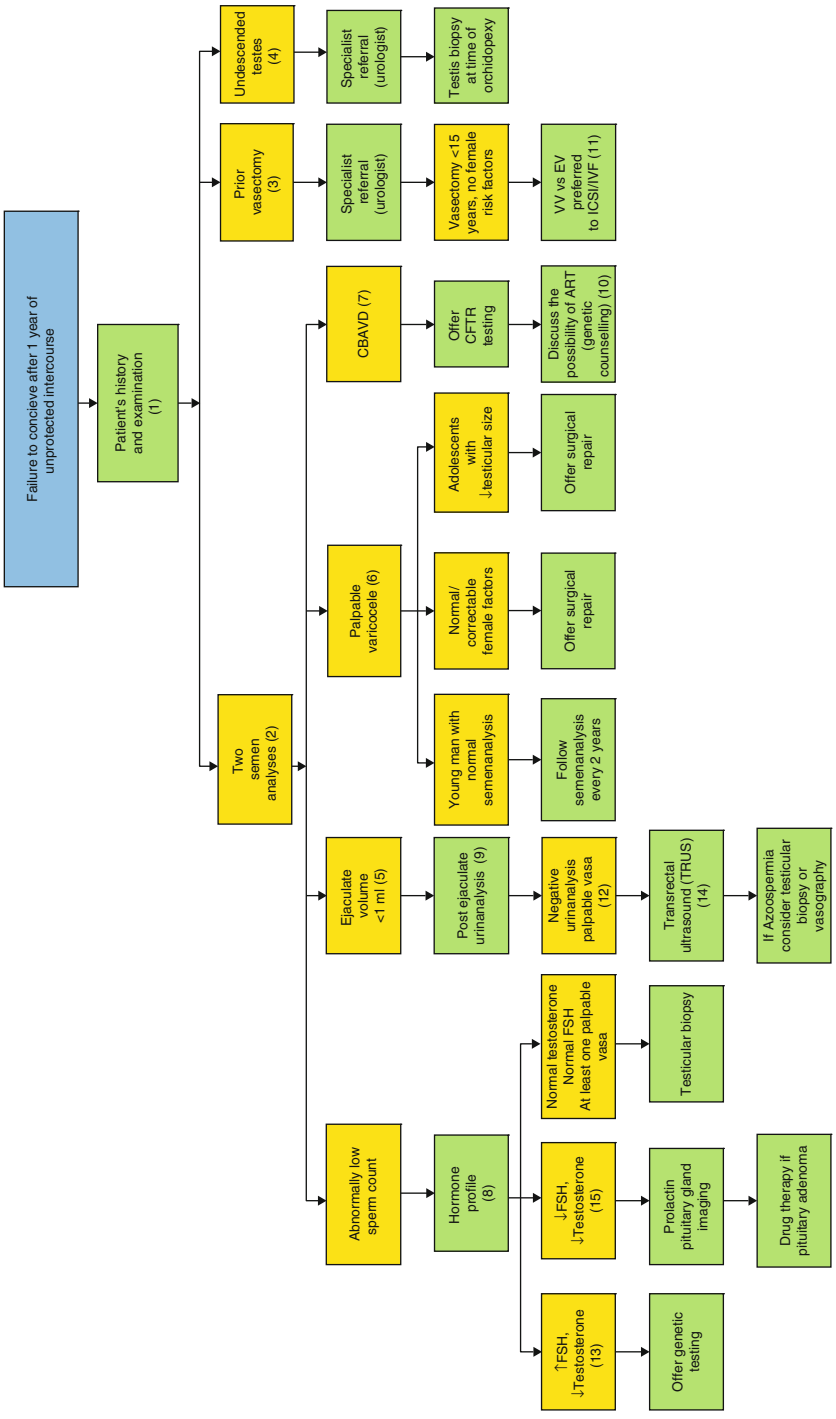
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WHO World Health Organization
[a]Lower reference limit obtained from lower fifth centile value
[b]Grade a, rapid progressive motility (>25 μm/s); grade b, slow/sluggish progressive motility (5–25 μm/s); normal, 50 % motility (grade a + b) or 25 % progressive motility (grade a) within 60 min of ejaculation
[c]Forward progression (scale 0–3)
[d]Arbitrary value
[e]Value not defined, but strict criterion (Tygerberg criteria) suggested

Management of Male Infertility in the GP Office

Comments About Flowchart 18.1

1. Patient's history of a male that has failed to conceive after 1 year of unprotected intercourse should focus on any previous surgery in the genital or inguinal area (hernia repair, varicoceles, orchidopexy, hypospadias repair, etc.), any delay in testicular descent during childhood, mumps orchitis or recurrent urinary tract and genital infections (particularly epididymo-orchitis), or exposure to toxic agents (chiefly chemotherapy or radiotherapy). A number of endocrine diseases may impair fertility and should thus be recalled. Notably, a number of androgen doping strategies aiming to increase testosterone levels can negatively affect testicular function.

 During examination it is of utmost importance to assess testicular and epididymal volumes and consistency. The vasa deferentia can usually be identified within the spermatic cord through manual palpation. The presence of varicocele and hernias should be ruled out.
2. Semen analyses should be taken after at least 73 h of abstention from ejaculation. Parameters of normal sperm count are presented in Table 18.1.
3. If a man has had a previous vasectomy less than 15 years prior to evaluation, microscopic vasovasostomy can be expected to produce viable sperm in more than 85 % of procedures. While men may have success after 15 years, the viable sperm outcomes are limited. In select patients, microscopic vasoepididymostomy may be successful.
4. In men with previously untreated cryptorchidism, orchidopexy is indicated if the testes are not easily palpable. If infertility is the indication for surgery, consideration should be given for testis biopsy at the time of orchidopexy to assess the sperm production and likelihood of a usable sperm production.
5. If ejaculate volume is less than 1 ml, retrograde ejaculation or vasal obstruction should be considered. Retrograde ejaculation is often observed in diabetics with neuropathy, men on alpha-adrenergic blockers, and men with previous prostate or bladder neck surgery.
6. Palpable varicocele is commonly associated with low sperm count, increased abnormal sperm, and reduced sperm motility. Microscopic varicocele repair can result in improved semen analysis parameters and enhanced fertility. Following surgery, semen analysis improvement may require follow-up of 6–12 months. While more varicoceles can be identified with imaging techniques such as ultrasound, the use of these techniques remains controversial.
7. Congenital bilateral absence of the vasa deferentia (CBAVD) is often associated with cystic fibrosis (CF). CF is the most common genetic abnormality in Caucasian men. CF is an autosomal-recessive disorder where 4 % are carriers of gene mutations involving the CF transmembrane conductance regulator (CFTR) gene. When a man has CBAVD, it is important to test him and his partner for CF mutations. If the female partner is a CFTR carrier, the couple may be at risk for CF offspring.



Flowchart 18.1 Failure to conceive after 1 year of unprotected intercourse

8. The usual hormone profile for the evaluation of male factor infertility includes total testosterone, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin. These may be supplemented by free testosterone and genetic counseling.
9. If ejaculate volume is less than 1 ml and there are risk factors for or a history of retrograde ejaculation, men should be asked to void and masturbate and the bladder aspirated to evaluate for the presence of sperm. Sperm can be harvested for artificial insemination in these men if retrograde ejaculation is demonstrated.
10. CF transmembrane conductance regulator (CFTR) gene testing for the patient and partner if CF or CBAVD is suspected can help with the decision to proceed with ICSI or other ART.
11. Microscopic vasovasostomy (VV) or vasoepididymostomy (EV) are microscopic surgical techniques that are frequently successful in restoring fertility with adequate sperm counts for conception. These procedures are cost effective and usually less expensive that advanced ART.
12. If the post ejaculation sperm count demonstrates no sperm, obstructive causes for the reduced volume should be considered. A transrectal ultrasound (TRUS) examination can be helpful in assessing the seminal vesicles and identifying obstructive abnormalities.
13. In men with abnormally low sperm counts, low testosterone and high FSH, Klinefelter's syndrome is a possibility and genetic testing may be helpful in confirming the diagnosis.
14. Transrectal ultrasound is a helpful technique in assessing the seminal vesicles, vasa, and ejaculatory ducts, as well as identifying abnormalities in the prostate and proximal lower urinary tract.
15. In men with low testosterone and otherwise normal hormone profile whose LH is normal or low, clomiphene citrate may be helpful in improving both testosterone and sperm count. If clomiphene citrate fails, HCG injections may produce improvements in sperm production. Men with pituitary adenoma may be treated with bromocriptine or more recently cabergoline or *quinagolide*.

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Chapter 19
Female Urinary Incontinence

Mary Garthwaite

Abstract Female incontinence is a common problem, which can have a significant impact on quality of life by leading to social exclusion, a sense of shame, and in some cases giving rise to symptoms of depression. It is often a hidden problem, as many women either feel too embarrassed to discuss their symptoms or merely see and accept it as an inevitable consequence of bearing children.

The three most common types of incontinence affecting women are stress urinary incontinence, urge urinary incontinence, and mixed urinary incontinence. It is important to be able to identify the type of incontinence from the symptoms described as the management of each differs considerably. The clinician must also have a clear understanding of the risk factors involved in the etiology of incontinence so that a holistic approach to management can be implemented.

This chapter aims to show how the initial assessment and treatment of women with urinary incontinence can be readily accomplished in the community when following a clear diagnostic algorithm. Appropriate referral on to specialist urological services is required when conservative measures fail.

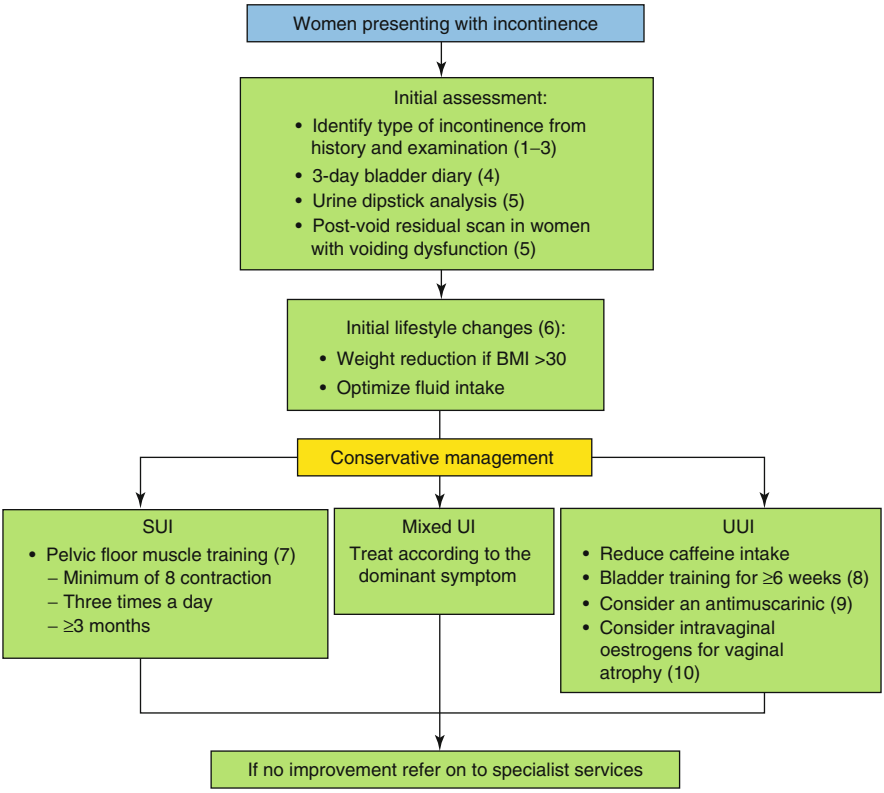
Keywords Stress urinary incontinence • Urge urinary incontinence • Conservative management

Introduction

Female urinary incontinence is a common problem, which can have a significant impact on quality of life by leading to social exclusion, a sense of shame, and in some cases giving rise to symptoms of depression. It is often a hidden problem, as

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Flowchart 19.1 An algorithm for the initial assessment and treatment of female urinary incontinence

many women either feel too embarrassed to discuss their symptoms or merely see and accept it as an inevitable consequence of bearing children.

The three most common types of incontinence affecting women are stress urinary incontinence (SUI), urge urinary incontinence (UUI), and mixed urinary incontinence (MUI). It is important to be able to identify the type of incontinence from the symptoms described as the management of each type differs considerably. It is also important to have a clear understanding of the risk factors involved in the etiology of incontinence so that a holistic approach to management can be implemented. Many cases of mild incontinence will respond well to basic lifestyle changes and conservative management strategies and will not require onward referral to specialist services.

The aim of this chapter is to offer clear and simple guidance on the initial assessment, investigation, and management of women presenting to their GP with incontinence.

Table 19.1 Common types of incontinence and the International Continence Society (ICS) definitions

Type of incontinence	Definition
Stress urinary incontinence	Involuntary loss of urine on effort or physical exertion or on sneezing or coughing
Urge urinary incontinence	Involuntary loss of urine associated with urgency
Mixed urinary incontinence	Involuntary loss of urine associated with urgency and also with effort or physical exertion or on sneezing or coughing

Table 19.2 Risk factors for urinary incontinence in women

Intrinsic	Environmental	Obstetric and gynecological
Family history	Age	Pregnancy and childbirth
Race	Obesity	Pelvic surgery
Neurological conditions (multiple sclerosis, Parkinson's disease)	Raised intra-abdominal pressure (chronic cough, exercise)	Pelvic radiotherapy
Anatomical abnormalities (congenital abnormalities, pelvic organ prolapse)	Urinary tract infections	
	Medication (diuretics, antidepressants)	
	Food stuffs (caffeinated or carbonated drinks, alcohol)	

Comments About Flowchart 19.1

1. A thorough history should allow the clinician to identify the likely type of incontinence based on the symptoms described by the patient. The International Continence Society (ICS) defines the symptom of urinary incontinence as the "complaint of involuntary loss of urine." Several types of incontinence are classified by the ICS, but the three most common types seen in women are SUI, UUI, and MUI (Table 19.1).
2. The prevalence of female incontinence increases with age. Several risk factors are thought to play a role in the etiology of urinary incontinence in women, and these include obesity, increased age, menopause, pregnancy and childbirth, pelvic organ prolapse, previous pelvic surgery/radiotherapy, urinary tract infections, and chronic cough. A list of risk factors for urinary incontinence is reported in Table 19.2. There may also be a family predisposition to incontinence or other predisposing factors such as neurological or anatomical abnormalities.
3. SUI may be evident on asking the women to cough or strain during genital examination. Vaginal examination allows assessment of pelvic floor muscle tone and the ability of the patient to correctly perform a pelvic floor contraction, as well as exclusion of significant pelvic organ prolapse as a causative factor. Initial examination should also include a quick assessment of perineal sensation and anal tone in order to exclude a neurological component to the incontinence.
4. A bladder diary, completed over three consecutive days, is useful in determining functional bladder capacity and the frequency and severity of incontinence as well as identifying frequency or nocturia secondary to an excessive fluid intake. It is a valuable tool in demonstrating to patients where simple lifestyle measures can be

implemented, such as moderating fluid intake and reducing caffeine consumption. An example of a bladder diary is reported in Chapter 13 (Table 13.2).

5. Urine dipstick analysis and bladder post-void residual measurement (using an ultrasound if available or by insertion of a small catheter) will help to differentiate patients who can safely be started on conservative management from those who may require immediate referral for specialist review. Urine dipstick analysis is recommended to exclude urinary tract infection or diabetes as possible causes of incontinence. A history of painless frank hematuria or persistent dipstick hematuria, so-called "red flag" signs, should trigger urgent referral to urology services for further investigation. A post-void residual volume is considered significant if it is greater than 30 % of total bladder capacity (usually >100–150 ml) on repeated assessment and should be recorded in all patients with a history of voiding dysfunction.
6. Depending on the type of incontinence, conservative management usually involves lifestyle interventions (reducing weight, optimizing fluid intake), behavioral strategies (bladder training), physical therapy (pelvic floor muscle exercises), or any combination of the three. Such measures are simple to implement, cost-effective, and low-risk initial treatment strategies that have the potential to provide significant improvement in incontinence symptoms. They do not work for all women, and their success often depends on the severity of symptoms, the level of available patient education and support, and long-term patient motivation and compliance. If symptoms fail to improve after a concerted period of conservative management, referral for specialist assessment and treatment should not be delayed.
7. Conservative management of SUI involves pelvic floor muscle training. This is recommended to include three sets of at least eight pelvic floor contractions a day, for at least 3 months. It is important to ensure that the patient can correctly identify and contract their pelvic floor muscles, rather than incorrectly performing a Valsalva maneuver. It is well known that initial instruction and then monthly follow-up with a specialist physiotherapist improve patient compliance.
8. Initial management of UUI may involve reducing caffeine intake if excessive and bladder training (also referred to as bladder drill). Bladder training aims to teach patients how to resist or suppress the desire to urinate and thereby help them improve their functional bladder capacity, decrease incontinence episodes, and regain control of bladder function. Techniques to help resist urgency include removing or avoiding causative stimuli (turn off taps, avoid sudden changes in temperature or position), distraction activities (counting backwards), and positional aids or perineal pressure (standing on tiptoe, sitting on arm of a chair, contracting pelvic floor muscles).

 The use of a strict voiding schedule can also be of benefit but requires a lot of patient motivation. Initially the patient is instructed to void every hour during the day, whether or not she has the desire to void. She must not void in between these times and consequently must either wait until the next scheduled void or be incontinent. If baseline bladder diaries indicate an average daytime voiding interval of less than 1 h, then a shorter initial voiding interval should be set. As each voiding interval target is reached, the scheduled interval is increased by 15–30 min each week until an interval of 2–3 h is reached. If no significant improvement is seen after 6 weeks, then bladder training should be abandoned and other treatment options considered.

9. If bladder training fails, then it is acceptable to consider a trail of an antimuscarinic in patients with no contraindications to their use, before referral on to specialist services. The NICE guidelines recommend the initial use of nonproprietary oxybutynin, followed by newer generation antimuscarinics such as solifenacin, tolterodine, or trospium. Transdermal preparations of oxybutynin are also available, with some studies reporting a lower incidence of dry mouth compared with oral preparations. However, this must be balanced against possible problems with localized skin irritation at the patch site.
10. If vaginal atrophy is clearly evident on vaginal examination, a short course of intravaginal estrogen (once daily for 2 weeks, then once or twice weekly for 2 months) can often improve symptoms of urgency and help in the management of UUI.

Conclusion

The initial assessment and treatment of women with urinary incontinence can be readily accomplished in the community when following a clear diagnostic algorithm. Appropriate referral on to specialist urological services is required when conservative measures fail or when preliminary tests raise "red flag" results.

When being referred for specialist review, patients should be aware that further assessment may involve more invasive tests, such as urodynamics and cystoscopy. Depending on the severity of the incontinence and the underlying cause, surgical management options for the treatment of SUI include midurethral tapes, fascial slings, colposuspension, periurethral bulking agents, and artificial urinary sphincter placement. Options for the treatment of UUI include intravesical botulinum toxin injections or sacroneuromodulation. All these procedures carry a greater risk to the patient, making it imperative that all conservative options available have been fully explored.

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Chapter 20
Male Urinary Incontinence

Simon Bugeja, Shafiullah Wardak, and Daniela Andrich

Abstract Urinary incontinence (UI) in men is a significant health and social issue with a reported incidence of up to 39 % especially with increasing age. The majority of sufferers can be managed safely and effectively by the primary health-care physician in the community. However, incontinence may also be the presenting feature of serious underlying pathologies such as bladder tumors or stones. It may also lead to significant complications if unrecognized or left untreated as in the case of chronic retention with overflow incontinence and its effect on the upper tracts eventually resulting in renal impairment. Besides it represents significant impact on the patient's quality of life and that of his carers.

This chapter provides a simple to follow algorithm which guides practitioners through the early assessment and investigation of men presenting with UI, providing them with a step-by-step approach to formulate a working differential diagnosis. Treatment pathways which should be initiated (conservative and pharmacological) are outlined. Most importantly, it helps identify those patients who need immediate referral for specialist urological care and also determine when to refer those whom they decide to manage primarily in the community.

We take the opportunity to describe in more detail the specialist management of post-prostatectomy incontinence with particular emphasis on the artificial urinary sphincter that represents its gold-standard surgical treatment. It is thus appropriate to provide primary care physicians with a greater understanding of how the device works, patient preparation, basic surgical principles involved, the routine course of events in the postoperative period, as well as what to look out for in terms of complications since most of these patients are discharged to follow-up in the community after having their sphincters implanted.

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Keywords Male urinary incontinence • Primary care • Post-prostatectomy incontinence • Sphincter weakness incontinence • Surgical management • Artificial urinary sphincter

Introduction

Urinary incontinence (UI), described by the International Continence Society as "the complaint of any involuntary leakage of urine," is a significant problem with reported prevalence rates of up to 39 %, especially with advancing age. International population-based surveys and a handful of prospective studies suggest a male to female ratio of 1:2. UI has an important impact on a patient's quality of life, those social, psychological, and sexual well-being, with potential significant occupational and financial consequences. It often has a major impact on nursing care. Three main types of UI can be recognised in men. 1) Sphincter weakness incontinence (SWI) defines unintentional urine loss, particularly during physical activity (walking, coughing, sneezing, excercise...). In this case the sphincter is not able to prevent urine from flowing when pressure is placed on the abdomen. 2) Urge urinary incontinence (UUI) is the inability to hold the urine following a strong, sudden desire to void. It usually results from reduced bladder compliance or detrusor overactivity. 3) Overflow incontinence (OI) defines urine dribbling in the presence of a distended bladder from chronic urine retention. Table 20.1 reports the main clinical conditions causing the 3 types of UI.

This chapter provides a practical algorithm to guide primary care physicians through the initial assessment and management of these men in the community on the one hand and on the other to identify those patients who need early urological opinion, in order to diagnose significant underlying pathology.

We take the opportunity to describe the more advanced management of sphincter weakness incontinence following prostate surgery, in particular the artificial urinary sphincter. This provides primary care physicians with a better understanding of how to manage these patients who are usually discharged to follow-up in the community, after having received specialized surgical treatment.

Initial Assessment and Management of Male Urinary Incontinence

Comments About Flowchart 20.1

1. The aim of initial assessment is to formulate a working differential diagnosis and identify those patients with complicated incontinence who need early referral to specialist care distinct from those who can be further assessed and safely managed in primary care. This should be based on a detailed history and physical examination. Table 20.1 lists a number of underlying urological and extraurological

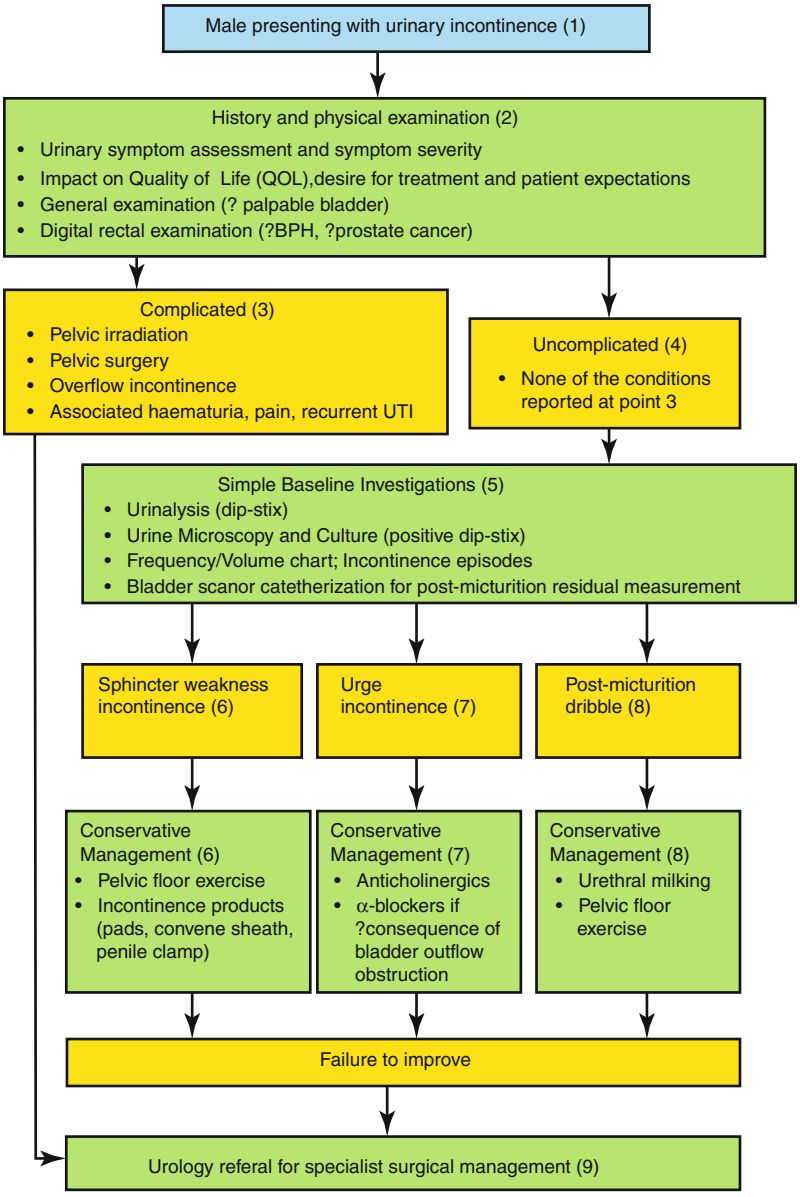
Table 20.1 Differential diagnosis of the three main types of male incontinence based on patient's history and associated urinary symptoms

History	Underlying pathophysiology	Type of incontinence
Associated voiding symptoms Poor/intermittent flow Hesitancy Post-micturition dribble Straining to void Spraying of stream	Bladder outflow obstruction (BPH; prostate cancer, urethral stricture) leading to chronic urine retention	Overflow incontinence (OI)
Associated storage symptoms pointing toward urge urinary incontinence (UUI) Frequency Urgency Nocturia	Associated with bladder outflow obstruction, idiopathic detrusor overactivity, secondary to bladder pathology (infection, cancer, stones)	Urge incontinence (UUI)
Associated hematuria, dysuria, pain, recurrent infections	Underlying bladder pathology (infection, cancer, stones)	UUI
Post-prostatectomy (transurethral resection for benign disease, radical prostatectomy for prostate cancer)	Damage of urinary sphincter	Sphincter weakness incontinence (SWI)
Post-pelvic surgery (e.g., radical cystectomy, anorectal resection)	Nerve injury leading to atonic bladder and sphincter weakness	SWI
Following pelvic radiotherapy	Small-capacity bladder, radiation cystitis, urinary sphincter damage, bladder neck contracture	UUI and/or SWI
Neurological conditions such as spina bifida, spinal cord injury, stroke, Parkinson's, diabetes	Neuropathic bladder – overactive/underactive bladder, overactive/underactive sphincter	Predominantly UUI
Other risk factors	Poor mobility, cognitive impairment, constipation, obesity, smoking, caffeine, medication (diuretics, anticholinergics)	All three types can occur alone or in combination

SWI sphincter weakness incontinence, *UUI* urge incontinence, *OI* overflow incontinence

diseases that may cause male urinary incontinence along with the patient's history and presenting symptoms.

2. History should assess the severity, precipitating factors, and impact of the UI on the patient's QOL. This will guide treatment selection and identify treatment goals. Severity is assessed by the number of urinary leakage episodes per day, daily pad use, and effect on activities of daily living. Validated questionnaires such as the International Consultation on Incontinence Questionnaire-Short Form



Flowchart 20.1 Male presenting with urinary incontinence

(ICIQ-SF) may help since they are easy to complete by the patient in the waiting room before their consultation. Incontinence in the context of other LUTS may be assessed by the International Prostate Symptom Score (IPSS) which also contains a QOL question.

Clinical examination should be focused on:

- General physical examination – to search for anemia and/or cachexia (suggestive of underlying malignancy) or signs of renal impairment
- Abdomen – to search for palpable bladder (suggesting urinary retention causing overflow incontinence), pelvic mass, loin fullness (hydronephrotic kidneys)
- Digital rectal examination (to assess prostate size, consistency, outline, tenderness), anal tone, pelvic floor muscle tone
- External genitalia
- Neurological examination (if a neuropathic bladder is suspected)

3. Men with incontinence following pelvic surgery or radiotherapy form a group of patients who often have severe symptoms and complex underlying pathologies. They are less likely to respond to conservative measures. Hence, they are classified as "complicated," warranting early specialist referral. They often need advanced investigation and management, commonly in a multidisciplinary team setup.

 UI in elderly men presenting to their general practitioners is commonly a result of bladder outflow obstruction secondary to BPH. This usually presents as a combination of urge urinary incontinence (UUI) and voiding symptoms in the early stages as the detrusor hypertrophies to overcome outflow resistance. In the later stages of the disease process, when the detrusor begins to decompensate, retention with overflow incontinence (OI) may result. Presentation is commonly dribbling incontinence, poor flow, frequent passage of small volumes of urine, nocturia, and urgency. OI must always be suspected in men with nocturnal incontinence.

 Typically retention with OI is painless and patients do not have a sensation of incomplete bladder emptying, so a high index of suspicion is necessary. Diagnosis is confirmed by a palpable bladder and/or post-void residuals >200–300 ml. These patients need early referral for expert urological management to prevent complications such as upper tract dilatation and renal impairment, recurrent infections, and bladder stones. They require decompression of the bladder by catheterization and surgical management of the underlying cause.

 OI in the elderly may also result from impaired bladder contractility secondary to medication (e.g., anticholinergics), neurological conditions (e.g., stroke), and peripheral neuropathy particularly in diabetics. Constipation, dementia, and limited mobility are all precipitating factors to this UI. If voiding fails after treating reversible causes, clean intermittent catheterization is the treatment of choice with an indwelling catheter only as a last resort.

 Men with UI and associated hematuria, pain, or recurrent infections suggestive of underlying bladder pathology (e.g., stones, tumors) should also have a low threshold for early specialist referral.
4. Those without a history of surgery, radiotherapy, hematuria, and pain, where overflow incontinence has been excluded, can be investigated further and managed accordingly by the primary care physician.
5. The following baseline investigations are recommended:
 - Urinalysis for blood, protein, glucose, leucocytes, and nitrites

- Urine culture and sensitivity to exclude infection
- A frequency/volume chart, where the patient is asked to record on a sheet the time, the urine volume for each micturition, as well as any episode of incontinence that occurred over 3 consecutive days (see Table 13.2 in Chap. 13)
- Post-void bladder scan, if ultrasound is available, or alternatively assessment of bladder residual volume through insertion of a small catheter may alert the practitioner to those patients with significant post-void residuals and increased risk of complications.

6. History can very often distinguish sphincter weakness incontinence (SWI) (on effort or exertion, sneezing, or coughing) from urge incontinence (UUI). This will guide further investigation and initial treatment.

 Men with uncomplicated incontinence, and not too bothersome symptoms, can be given reassurance and advice on simple lifestyle interventions such as fluid and caffeine intake, timed voiding (try and keep the bladder as empty as possible), weight loss, smoking cessation, and bladder training (hold on longer in UUI). Men with SWI should be referred for a trial of pelvic floor exercises and reassessed a few months later. They should be referred early for consideration of devices such as pads or convene sheaths to achieve "social continence" until diagnosis and a management plan are made.
7. In men with UUI, if significant post-void residuals are excluded by a simple bladder scan, treatment may be initiated with alpha blockers and the addition of 5-alpha reductase inhibitors if the prostate is very large. However, the mainstay of conservative management in men with uncomplicated UUI is anticholinergic medications. These work by blocking muscarinic receptors in the bladder wall with the end result being a reduction in detrusor contraction. Coexisting bladder outflow obstruction may precipitate acute retention, so patients must be advised to stop the medication immediately if they notice problems in voiding. Starting a low dose and titrating according to response is an option. Common side effects are constipation and a dry mouth. They are contraindicated in narrow-angle glaucoma. Several anticholinergics are available with no concrete evidence favoring one over the other. They do however demonstrate a different incidence of side effects. Failure to respond/tolerate one may be an indication to try a different one (see Table 13.5 on Chap. 13 for more details on anticholinergic drugs).
8. Post-micturition dribble is the involuntary leak of urine immediately after finishing voiding or just after leaving the toilet. It is caused by weakness of the bulbospongiosus muscle to completely expel urine which pools in the bulbar urethra. This can often be managed by pelvic floor exercises and manually compressing the urethra behind the scrotum after micturition (urethral milking).
9. The urologist will organize more detailed investigations (bladder/upper tracts ultrasound, flow rate, endoscopy, video urodynamics) based on the findings in the history and clinical examination in order to reach a diagnosis and institute treatment accordingly.

Surgical Management of Post-prostatectomy Incontinence (PPI)

UI occurs in around 1 % of cases following transurethral resection of the prostate (TURP). The incidence is higher and more variable following radical prostatectomy (5–48 %), but the overall incidence is on the decline. The commonest underlying pathological processes are SWI, detrusor overactivity (DO), or a combination of both. DO would have commonly been identified prior to referral and treated conservatively with anticholinergics. Most would have failed a trial of pelvic floor exercises. We will therefore focus our attention on the surgical management of SWI post-prostatectomy.

History, examination, and basic investigation are similar to men with UI in general. Special attention is paid to symptom severity, ability to void normally between incontinence episodes, associated storage, and voiding symptoms.

Treatment options are summarized in Table 20.2. The gold standard is the artificial urinary sphincter (AUS). Its efficacy has been demonstrated in the long term. The AMS 800™ is the most commonly implanted sphincter (Fig. 20.1a). It is a 3-component device consisting of a cuff positioned around the bulbar urethra, a pump implanted into a subcutaneous dartos pouch in the scrotum, and a reservoir balloon placed extraperitoneally in the groin (Fig. 20.1b). The sphincter works on the principle that fluid from the reservoir is filling the cuff, transmitting an occlusive pressure onto the urethra. Squeezing the pump shifts fluid from the cuff into the reservoir, thereby opening the cuff, allowing unobstructed voiding.

Adequate dexterity to manipulate the pump is a prerequisite for sphincter implantation. If patients are able "to do up their shirt buttons," then this is adequate. Sterile urine must be ensured preoperatively since device infection spells disaster. Bladder neck or urethral strictures must be excluded by antegrade/retrograde urethrography or endoscopy and treated by dilatation, incision, or urethroplasty. Video urodynamics are performed if there is suspicion of a small-capacity bladder or DO with high

Table 20.2 Surgical options for post-prostatectomy incontinence

Treatment	Comments
Periurethral bulking agents	Limited efficacy
	Only temporary solution
	Only in mild SWI following prostatectomy
	No one agent better than the other
Male slings	Gaining popularity due to minimally invasive procedure (for mild to moderate SWI)
Fixed	Predetermined urethral compression cannot be modified, e.g., InVance, AdVance (poor outcome in severe SWI, post-radiotherapy)
Adjustable	Tension in sling can be adjusted postoperatively, e.g., Reemex, Argus (no benefit over fixed slings)
Artificial urinary sphincter	Gold-standard management for moderate to severe SWI (*see text*)

bladder pressures. Patients are counseled that storage symptoms may develop, persist, or (occasionally) worsen once the device is in place. Significant unstable bladder contractions >30–40 cmH_2O may overcome the occlusive cuff pressure resulting in urine leakage, hence the aim to control DO beforehand using anticholinergic medication.

Patients are allowed to handle a demonstration device in clinic and are given patient information leaflets. The cuff is inserted through a perineal midline incision, while the reservoir and pump are inserted through a separate groin incision. A catheter is left in situ and removed the following morning. Patients go home when voiding satisfactorily with minimal bladder residuals. The device is deactivated (i.e., cuff open) at the time of surgery, so they need to continue using continence appliances until it is activated (i.e., cuff closed, filled with fluid) 6 weeks later. By this time pain and scrotal swelling should have settled so the pump can be manipulated comfortably. Patients are shown how to cycle the pump (i.e., only to squeeze the lower part of the pump avoiding the deactivation button) to open the cuff and are allowed home after having voided and demonstrating satisfactory handling of the device.

A device patient identification card is provided containing implantation center contact details. All health-care professionals in contact with the patient should be

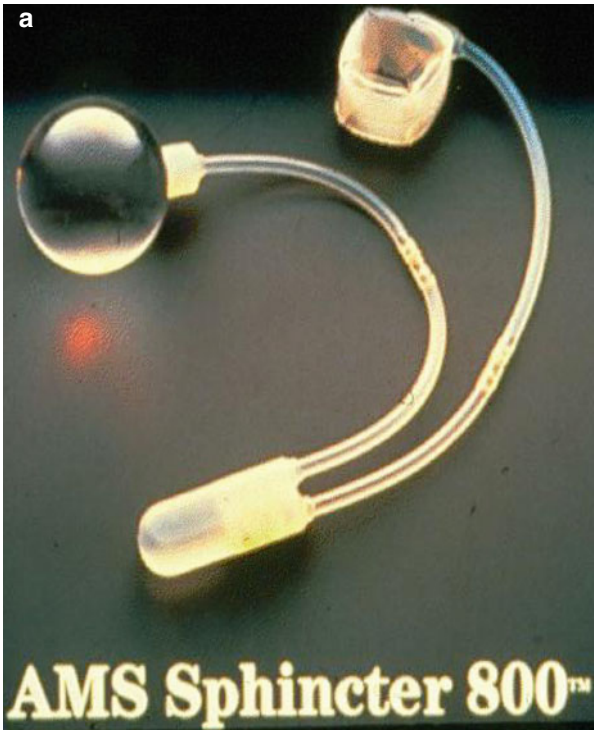


Fig. 20.1 (**a**) AMS800TM artificial urinary sphincter and (**b**) diagrammatic representation of implanted components (Adapted from Hussain et al. (2005). With permission from Elsevier)

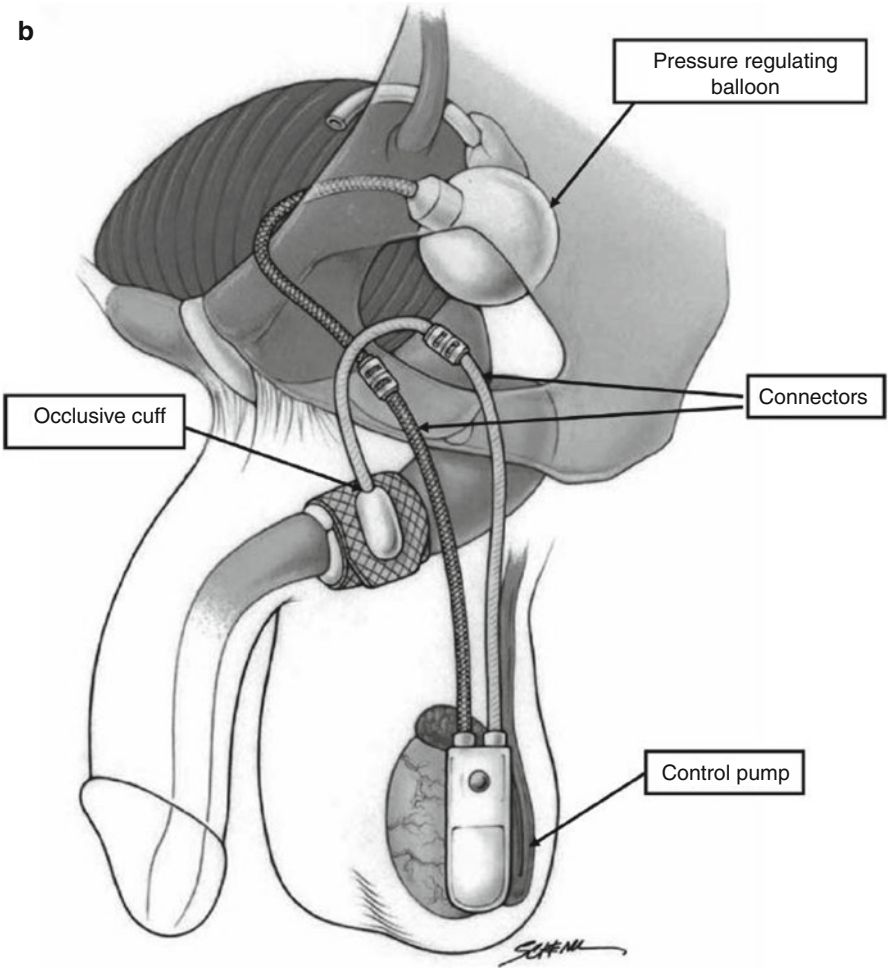


Fig. 20.1 (continued)

aware that an AUS is in place. If urethral instrumentation becomes necessary, the device should be deactivated beforehand! We discharge patients from specialist follow-up after a satisfactory 4-month checkup provided there were no underlying complicating factors such as bladder neck stenosis. Most patients are very satisfied with the AUS, achieving continence rates of >85 % at 10 years, being either dry or down to one "safety" pad/day. The device is usually reliable with a mechanical failure rate of around 30 % at 10 years.

The main complications of the AUS are outlined in Table 20.3. Device infection and/or erosion are the most serious, and when suspected, immediate referral back to the implanting surgeon is warranted since if confirmed, the device must be explanted as soon as possible to avoid unnecessary further damage to the urethra.

Table 20.3 Complications of the artificial urinary sphincter

Complication	Comments
Infection	Usually an early complication 7–10 days post-op
	Erythema, swelling, tenderness, pain over components
	Not eradicated by antibiotics
	Needs to be explanted as soon as possible
	Can be replaced 3–6 months later if urethra not too damaged
Erosion	Commonly associated with infection
	Painful voiding, worsening incontinence, sometimes retention
	Needs to be explanted as soon as possible
	Can be replaced 3–6 months later if urethra not too damaged
Mechanical failure	Presents as recurring SWI
	Most commonly due to cuff crease stress puncture
	Leakage of fluid is thereby leading to loss of pressure in the system
	Can be confirmed by an empty pressure-regulating balloon on X-ray or ultrasound
	Treated by replacement of device at same time of explantation if infection/erosion was excluded

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Part II
Decision Making Based on Objective Examination or Investigational Findings

Chapter 21
Enlarged Prostate (On Digital Rectal Examination or Ultrasound)

Bilal Chughtai, Dean Elterman, Richard Lee, Alexis Te, and Steven Kaplan

Abstract A common complaint of the aging male will be symptoms associated with benign enlargement of the prostate gland. These lower urinary tract symptoms (LUTS) may be categorized as either irritative (frequency, urgency, nocturia) or obstructive (hesitancy, weak stream, straining, and prolonged voiding). Benign prostatic hyperplasia (BPH) is the underlying histologic cause of LUTS, caused either by direct bladder outlet obstruction (BOO) or increased smooth muscle tone. A basic algorithm may be followed to evaluate male LUTS including relevant medical history, assessment of LUTS, validated questionnaires on severity and bother, physical examination, DRE, serum PSA, and voiding diaries. Part of routine screening is a DRE (digital rectal examination), which allows for detection of nodules, asymmetry, and size. An enlarged prostate on DRE is common in the aging male and should prompt further evaluation for voiding symptoms. Ultrasound assessment of the enlarged prostate, most commonly transrectal ultrasound (TRUS), aids in the determination of size and response to therapy and in the guidance of directed prostate biopsies but has limited role in the assessment of prostate malignancy. The use of prostate-specific antigen (PSA) and enhanced imaging modalities, such as CT and MRI, replaced TRUS in the diagnosis of prostate cancer. The first-line agent in patients with an enlarged prostate less than 40 g in size and bothersome LUTS is alpha-blockers. There are currently multiple treatments available for men with enlarged prostate and LUTS, including alpha-adrenergic receptor antagonists, 5-alpha reductase inhibitors, anticholinergics, and combination therapy. It is important to approach each patient individually, focusing on history, physical examination, and laboratory tests. Assessment parameters (symptom scores, uroflowmetry, and prostate size) may help in identifying men at greater risk of progression who may benefit from more aggressive medical management using combination therapy.

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Keywords Benign prostatic hyperplasia (BPH) • Enlarged prostate • Lower urinary tract symptoms • Transrectal ultrasound (TRUS) • Digital rectal examination (DRE) • Management

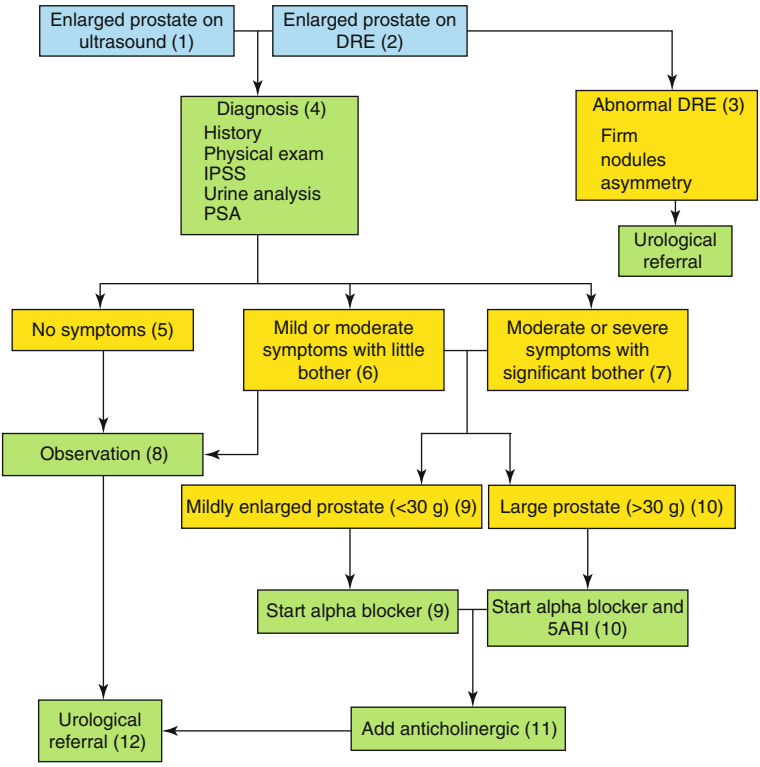
Introduction

Most men, within their lifetime, will develop prostate gland growth. In the majority of cases, this event is due to a para-physiological event known as benign prostatic hyperplasia (BPH). Susceptibility to male hormones (androgens) as well as a number of molecular events currently not yet understood is thought to sustain BPH that affects up to 70 % of adults or elderly males. Prostate enlargement may also be due to a malignant growth within the prostate. Early detection of prostate cancer as a result of PSA screening in Western countries has led to identify low-volume prostate cancers, thus reducing the number of patients diagnosed with an enlarged prostate due to cancer. While some men with an enlarged prostate are mostly asymptomatic and virtually unaware of their prostatic growth, a significant proportion of them will complain of variable degrees of one or more urinary symptoms currently termed as "lower urinary tract symptoms" (LUTS). In these cases, direct mechanical compression of the prostatic urethra and increased smooth muscle tone secondary to bladder outlet obstruction (BOO) are the most common physiopathological events leading to LUTS that are usually categorized as either irritative (frequency, urgency, nocturia) or obstructive (hesitancy, weak stream, straining, and prolonged voiding). A basic algorithm to evaluate a male presenting with LUTS has already been described elsewhere in this book (see Chap. 13). This chapter will instead address another common clinical scenario, that is, men presenting to the GP with the incidental finding of an enlarged prostate during a routine pelvic ultrasound or found to have an enlarged prostate during a digital rectal examination (DRE) performed by the GP. DRE is an essential part of the routine screening of prostate which allows for detection of nodules, asymmetry, and size. Ultrasound assessment of enlarged prostate aids in the determination of size and response to therapy and in the guidance of directed prostate biopsies but has limited role in the assessment of prostate malignancy. Herein we discuss the basic assessment of the enlarged prostate including the role of ultrasound.

Management of Enlarged Prostate

Comments About Flowchart 21.1

1. Occasionally patients present to the GP concerned by the ultrasound finding of an enlarged prostate. Irrespective of the ultrasound methodology employed (suprapubic or transrectal), early BPH presents as symmetric, homogeneous, hypoechoic areas superior and anterolateral to the verumontanum. Growth continues through the anterior paraurethral transition zone (TZ) eventually forming a nodular



Flowchart 21.1 Enlarged prostate on ultrasound or DRE

heterogeneous pattern of adenoma. The "surgical capsule" is the hypoechoic band of fibromuscular stroma compressed by the outer smooth muscle of the urethra. When the TZ grows outwardly, it can compress the peripheral zone (PZ) into a thin crescent of tissue, distorting the prostatic contour. Ultrasound measurements can follow the natural history of BPH as well as therapeutic response to medical management. When used for other indications, ultrasound may incidentally detect bladder calculi, large capacity bladders in occult urinary retention, hydronephrosis, upper tract calculi, renal masses, or abdominal aortic aneurysms.

Transrectal ultrasound (TRUS) does provide good-quality images of the prostate gland using high-frequency probes close to the prostate within the rectum. TRUS-visible lesions have been found in more than 50 % of patients with impalpable prostate cancer. Prostate cancer is usually seen as a hypoechoic area in the peripheral zone. It can rarely be seen as a hyperechoic area as well. Concerningly, up to 40 % of prostate cancers appear isoechoic (the same as surrounding normal tissue). Also, hypoechoic areas within the peripheral zone are not specific to prostate cancer and may be a benign process, such as prostatitis, infarction, or atrophy. In fact, hypoechoic lesions have a 17–57 % chance of being malignant. TRUS evaluation of prostate cancer can be altered by marked BPH, which produces a heterogeneous pattern of hyperplastic nodules compressing the peripheral zone,

making interpretation difficult. Most cancers are located in the peripheral zone; therefore, a hypoechoic lesion along the capsule is more suspicious than a heterogeneous BPH lesion in the transition zone. Given its poor sensitivity and specificity, TRUS has a limited function in cancer detection. TRUS is no longer used as the main modality in the assessment of prostate cancer. The use of prostate-specific antigen (PSA) and enhanced imaging modalities, such as CT and MRI, has downgraded the role of TRUS in the diagnosis of prostate cancer.

2. Routine evaluation of every male includes a digital rectal examination (DRE). An enlarged prostate is not an atypical finding in the aging male. An enlarged prostate may lead to voiding symptoms by two theoretical routes. It may limit the urine flow through direct obstruction and secondarily by increasing the muscular tone of the prostate. With a finding of an enlarged prostate, it becomes prudent to evaluate a patient for voiding symptoms.
3. The physical examination should also include a prostate exam to evaluate size and the presence of nodules. The finding of asymmetry, firmness, or nodules should trigger a referral to a urologist for management of a possible prostate cancer. The prostate should also be assessed for tenderness, as this may represent acute prostatitis that may need to be treated with antibiotics.
4. The assessment of any man who presents with a finding of an "enlarged prostate" should begin with the medical history. The medical history should include any causes that may lead to bladder dysfunction including cerebral vascular accidents, neurologic disorders such as Parkinson's or multiple sclerosis, previous surgical procedures or trauma, and history of prostate disease. A complete review of patients' medications is necessary.

 Next on history is the specific assessment of LUTS, as the management of an enlarged prostate that is not suspicion for malignancy will depend upon the presence or not of symptoms and/or complications. The presence and degree of severity of LUTS can be assessed using validated measures and questionnaires, namely, the International Prostate Symptoms Score (IPSS) which has been reported in Chapter 13 in Table 13.3. The IPSS is available in several languages and has been validated in multiple populations. Scores of 0–7 categorize mild LUTS, 8–19 moderate and 20–35 severe LUTS. The endorsements of certain findings on history and/or physical examination point toward the presence of "complicated" LUTS. These include suspicious DRE, hematuria, abnormal PSA, pain, infection, palpable bladder, or neurological disease. In these instances, a referral to a urologist for more detailed management is indicated prior to the commencement of any treatment.

 Following the detailed medical history, the physician should proceed with a general and focused physical examination. Physical examination should always include an abdominal examination assessing for a palpable bladder, which may be a sign of urinary retention. Attention for hernias, surgical scars, and genital abnormalities should be paid. Fresh urine or a rash around the genitals may be a sign of urgency incontinence from overactive bladder or overflow incontinence from urinary retention (see Chap. 20 for more details on male urinary incontinence). Physical examination should always include a digital rectal examination (DRE).

All men should get a urinalysis to rule out the presence of blood or urinary tract infection. The opportunity for a PSA test may be discussed (see Chap. 24).

5. Those men with an enlarged prostate and minimal clinical symptoms as per the IPSS (≤7 points) can often be observed. These men can be advised about behavioral modifications including fluid restriction, timed voiding, and double voiding. Observation can also be advised to those with moderate symptoms (8–19 points in the IPSS) with minimal bother. These patients do require periodic revaluation to avoid recurrent infection, bladder stones, urinary retention, refractory hematuria, or renal dysfunction.
6. In general, patients with mild symptoms (IPSS 0–7) or those with moderate symptoms (IPSS 8–19) with little bother should be monitored and periodically reassessed. Those with moderate or severe symptoms should be offered some form of medical therapy. This IPSS however does not replace a discussion with a patient in regard to their voiding symptoms.
7. Those men with an enlarged prostate and minimal clinical symptoms as per the IPSS (≤7) can often be observed. These men can be advised about behavioral modifications including fluid restriction, timed voiding, and double voiding. Observation can also be advised to those with moderate symptoms (8–19 points) with minimal bother. These patients do require periodic reevaluation to avoid recurrent infection, bladder stones, urinary retention, refractory hematuria, or renal dysfunction.
8. Many natural agents falling under the name of "phytotherapy" (herbal-derived compounds) have been used for LUTS due to BPH. At the moment there is little evidence in support of their efficacy in spite of the good tolerability profile. Phytotherapy is an optional and well-tolerated treatment option that can be used alone for mild LUTS due to BPH or in combination with alpha-blockers for moderate to severe symptoms. Conventional drugs currently available for symptomatic BPH are listed in Table 21.1.
9. The first-line agent in patients with an enlarged prostate less than 30 g in size and bothersome LUTS is alpha-blockers. Alpha-blockers decrease bladder outlet resistance provided by urethral smooth and possibly striated sphincter tone to alleviate LUTS. As a class, alpha-blockers have a side effect profile that includes orthostatic hypotension and dizziness. The use of alpha-blockers may result in retrograde ejaculation. All medications in this class should be stopped prior to cataract surgery for fear of intraoperative floppy iris syndrome, which may make cataract extraction particularly difficult.

Table 21.1 Conventional agents commonly used for symptomatic BPH. See also Table 13.5 in Chapter 13 for more details

Alpha-blockers	Anticholinergics	5 α-reductase inhibitors (5-ARIs)
Tamsulosin	Oxybutynin	Finasteride
Terazosin	Tolterodine	Dutasteride
Alfuzosin	Trospium	
Silodosin	Darifenacin	
Doxazosin	Solifenacin	
	Fesoterodine	

10. Prostate growth is an androgen-dependent process. 5-ARIs (5-alpha reductase inhibitors) were developed to block the conversion of testosterone to dihydrotestosterone, thus reducing prostate volume and thereby decreasing bladder outlet obstruction. The two commonly used medications are finasteride and dutasteride, the former of which competitively inhibits 5α-reductase type 2 and the latter of which inhibits both subtypes. Side effects include erectile dysfunction, reduced libido, and decreased ejaculate volume in 5–10 % of patients, and breast enlargement and tenderness may occur in 1–2 % of patients.

 5-ARIs therapy can be combined with alpha-blockers. In a large multicenter, randomized, double-blind study of 4,844 men, the efficacy of combination therapy of dutasteride and tamsulosin in patients with LUTS and an enlarged prostate (prostate volume >30 ml) revealed that combination therapy improved voiding symptoms at 24 months. Combination therapy was more effective than monotherapy in treating LUTS in men with prostate volumes above 30 cm^3. Moreover, combination therapy led to significant increases in patient-reported, disease-specific quality of life measures.

 Although 5-ARIs in combination with alpha-blockers decrease both prostate volume and symptoms, with cessation of 5-ARIs, the prostate gland enlarges and symptoms reoccur. 5-ARIs should be prescribed indefinitely for severe symptoms or larger prostates.
11. Men with enlarged prostates typically present with a combination of irritative and storage LUTS. Often, LUTS seen with an enlarged prostate result in changes in detrusor function leading to overactivity. This latter condition is ameanable to treatment with anticholinergic drugs (Table 21.1). There has been a reluctance to prescribe antimuscarinics to men with enlarged prostates with predominately irritative symptoms for fear of decreasing bladder contractility in the setting of bladder outlet obstruction. However, multiple trials have supported the safety and efficacy of these medications in treating men with enlarged prostates.
12. There are currently multiple treatments available for men with enlarged prostate and LUTS, including alpha-adrenergic receptor antagonists, 5-ARIs, and anticholinergics. It is important to approach each patient individually, focusing on history, physical examination, and laboratory tests. Assessment parameters (IPSS symptom score, uroflowmetry, and prostate size) may help in identifying men at greater risk of progression who may benefit from more aggressive medical management using combination therapy. Patients with severe LUTS not responding to medical therapy deserve a urological referral. In addition, patients who have a suspicious DRE, hematuria, abnormal PSA, pain, infection, palpable bladder, or neurological disease should be referred to a urologist.

Conclusion

An enlarged prostate is a common finding affecting the majority of adult and elderly men. It is important to emphasize that not all large prostates require treatment. Large prostates with little or no accompanying LUTS can be managed with observation.

Several drugs are available for treating moderate to severe LUTS associated with an enlarged prostate. A urological referral should be sought in the case of abnormal findings on DRE, the presence of BPH complications (hematuria, UTI, urine retention), or persistence of bothersome LUTS in spite of medical therapy.

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Chapter 22
Renal Stone on USS/X-Ray

Arun Sahai, Andrew Symes, and Jonathan M. Glass

Abstract The lifetime prevalence of kidney stones in the UK is thought to be approximately 5–12 %. Men are affected two to three times more commonly than women. Peak incidence occurs in the mid-20s and in the fourth to sixth decades. Following a stone episode, 50 % of patients will form another stone within 10 years. Stone formation depends on a number of extrinsic factors such as geography, climate, season, water intake, diet, and occupation. Treatment will depend on symptoms, size, anatomy, infection, and etiology. Not every renal stone, particularly those that are small and asymptomatic, necessarily needs a urological referral. Rather, patients can be effectively managed and followed up by the GP. Some renal stones will need emergency admission if, for example, there is sepsis associated with the stone or if there is pain. We propose a simple algorithm to help facilitate the decision-making process for community practitioners in managing renal stones. Symptomatic patients, patients with stones size >5 mm, or those with certain risk factors will need referral to the local urologist. We feel asymptomatic patients with a solitary nonobstructing renal stone <5 mm could be managed in the community and be monitored with an easy route into secondary care if necessary.

Keywords Renal calculus • Renal stone • Urolithiasis • Ultrasound • KUB X-ray • Renal stone guideline

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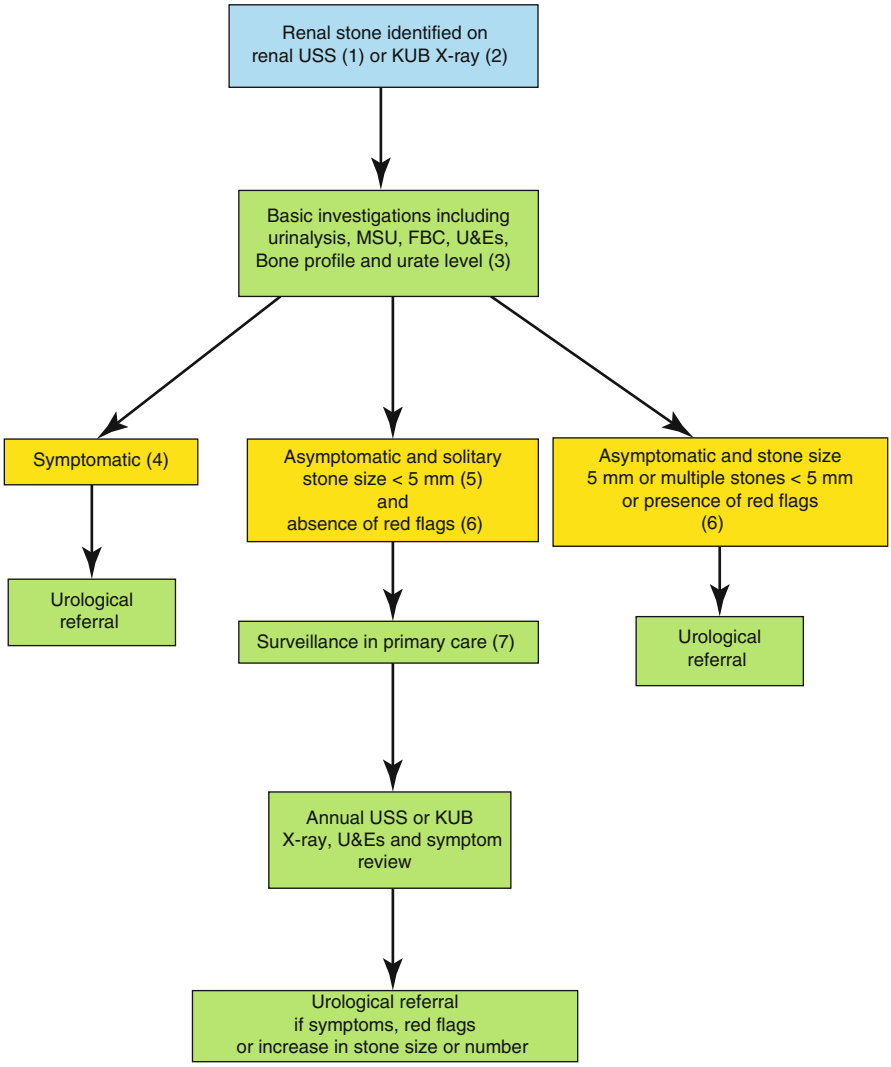
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Introduction

The lifetime prevalence of kidney stones in the UK is thought to be approximately 5–12 %. Analyzing hospital episode statistics data from the last 10 years, the prevalence rates and interventions for stone disease are increasing year on year. Men are affected two to three times more commonly than women. Peak incidence occurs in the mid-20s and in the fourth to sixth decades. Following a stone episode, 50 % of patients will form another stone within 10 years. Stone formation depends on a number of extrinsic factors such as geography, climate, season, water intake, diet, and occupation. Renal stone composition and stone size can be variable with stones from 1 mm to those measuring a few centimeters involving the renal pelvis and calyceal system (staghorn stones). Treatment will depend on symptoms, size, anatomy, infection, and etiology. Not every renal stone, particularly those that are small and asymptomatic, necessarily needs a urological referral. Rather, patients can be effectively managed and followed up by the GP. Some renal stones will need emergency admission if, for example, there is sepsis associated with the stone or if there is pain. The aim of this chapter is to provide a practical algorithm as to which patient should be referred to secondary care and to provide basic information for the work-up of those patients that can be managed by the GP. Furthermore, the comments will highlight important aspects of the decision-making process in more detail.

Comments About Flowchart 22.1

1. Renal calculi may be picked up on a variety of imaging modalities. Increasingly stones are being picked up on scans performed for other reasons, typically to investigate abdominal pain. The EAU guidelines state that if kidneys, ureter, and bladder (KUB) ultrasound (US) is available, this should be used as the primary diagnostic imaging tool although pain relief or any other emergency measures should not be delayed by imaging assessments. The advantages of KUB US are that it is safe (no radiation), it is generally reproducible (albeit being an operator-dependent technique), it is inexpensive, and it can be safely used in pregnancy. It can identify stones located in all parts of the kidney and can detect hydronephrosis. Typically stones are seen as hyperechoic (bright) on KUB US and cast a posterior acoustic shadow (Fig. 22.1). For stones >5 mm, ultrasound has a sensitivity of 96 % and specificity of nearly 100 %, but when assessing all stone locations, sensitivity and specificity of ultrasound reduce to 78 and 31 %, respectively. Noncontrast helical computerized tomography (CT) has gained widespread acceptance in the diagnostic work-up of urinary tract stones. Sensitivity and specificity of CT KUB in detecting stones are 92–100 and 94–100 % (Fig. 22.2), respectively. In secondary care this has largely superseded the use of US and intravenous urography in the acute setting and may be increasingly used in a primary care setting. Advantages of CT KUB include possible detection of other pathology or alternative diagnoses as well as being rapid to perform and much less operator dependent than KUB US.
2. Not all stones are radiopaque. A summary of stone compositions and their X-ray characteristics are outlined in Table 22.1. The sensitivity and specificity of KUB



Flowchart 22.1 Renal stone on USS/X-ray

X-ray are 44–77 and 80–87 %, respectively. KUB X-rays are useful in following up patients with radiopaque stones or after intervention to assess stone burden. However, its use in the acute setting is being superseded by CT KUB (see point 1). Approximately 75 % of all stones contain calcium. The commonest stone type is calcium oxalate contributing to approximately 60 %, followed by a mixture of calcium oxalate and calcium phosphate with 20 % and brushite 2 %. Uric acid and magnesium ammonium phosphate stones both contribute approximately

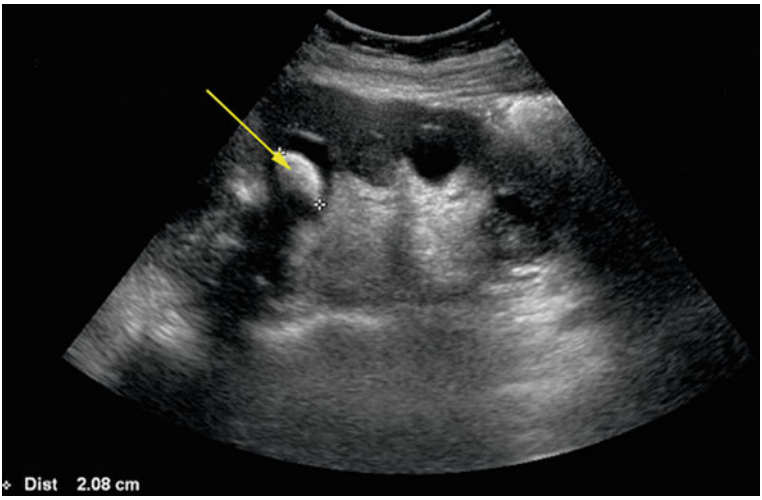


Fig. 22.1 Typical appearance of a renal calculus (*yellow arrow*) on US imaging with acoustic shadowing

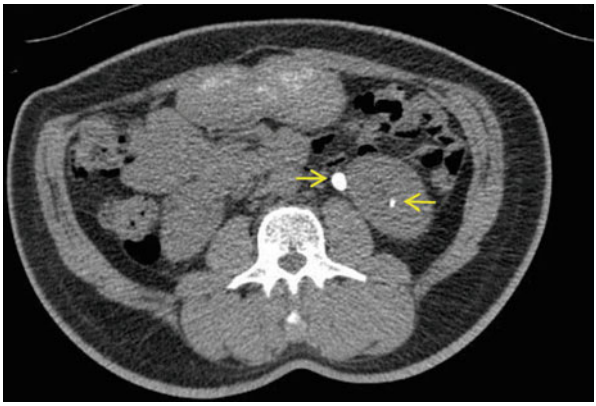


Fig. 22.2 CT scan showing a stone in the upper ureter on the *left* and a small stone in the lower pole on the *same side* (*yellow arrows*)

7 % each. The remainder of stone types is related to genetic/hereditary disorders such as cystinuria, hyperoxaluria, and xanthinuria.

3. Patients who are thought to have kidney stones or have an incidental renal stone identified should undergo a thorough history, examination, and basic investigations. In the history, an assessment for risk factors for stone disease should be sought (see Table 22.2). Thirty-five to fifty percent of stone formers will have a family history of stone disease. The investigative work-up includes screening for infection with urinalysis, a midstream urine specimen, and blood tests. These latter include a full blood count (to screen for infection and obtain a baseline hemoglobin); urea, electrolytes (U&Es) and creatinine to assess renal function; and a basic metabolic profile including calcium, urate, and phosphate level.

Table 22.1 Typical stone composition and X-ray characteristics

Radiopaque	Poor radiopacity	Radiolucent
Calcium oxalate dihydrate	Magnesium ammonium phosphate	Uric acid
Calcium oxalate monohydrate	Apatite	Ammonium urate
Calcium phosphates	Cystine	Xanthine
		2,8-Dihydroxyadenine
		Certain drug-related stones, e.g., indinavir, triamterene

Table 22.2 Risk factors for stone disease

Risk factor	Mechanism
Diet	Poor fluid intake, fluid type, meat consumption
UTIs	Urease-producing bacteria, e.g., Proteus and Klebsiella predispose to magnesium ammonium phosphate stones
Aberrant anatomy	Pelvi-ureteric junction obstruction, ureteric stricture, horseshoe kidney, medullary sponge kidney
Systemic/metabolic disease	Gout, primary hyperparathyroidism, sarcoidosis, tuberculosis
Drugs	E.g., chemotherapy, steroids
Poor mobility	E.g., spinal injury patients, spina bifida
Bowel condition resulting enteric hyperoxaluria	Bowel resection, inflammatory bowel disease
Genetic/hereditary conditions	Cystinuria, xanthinuria, renal tubular acidosis
Foreign material	Stents, suture material

4. Patients with urinary stones usually present with loin pain, vomiting, nausea, and sometimes fever (see Chap. 1) but may also be asymptomatic. Symptomatic patients with persistent pain or evidence of sepsis from the history, for example, recent onset of rigors and pyrexia with a suspected or known renal stone, will need admission to secondary care and therefore prompt discussion with the urology team at the local hospital. Obstruction of the urinary system with infection is a urological emergency. In those with a small stone and no obstruction or in those being worked up for possible renal stone, it is important to consider other possible diagnoses. The vast majority (85–90 %) of stone formers have microscopic hematuria. If this is not present, there should be a low threshold to consider alternative etiologies for the symptom complex. Loin pain or left- or right-sided abdominal pain may indicate a ruptured abdominal aortic aneurysm in an elderly patient who is hypotensive. Other possibilities include pyelonephritis, pelvi-ureteric junction obstruction, renal trauma, diverticulitis, cholecystitis/biliary colic, appendicitis, bowel obstruction, peptic ulcer disease, lower lobe

Table 22.3 Red flags for asymptomatic urinary stone warranting urological referral

Hydronephrosis
Pregnancy
Renal failure
Solitary kidney
Recurrent urinary tract infections
Congenital urinary tract anomalies (e.g., horseshoe kidney)
Urinary tract reconstruction (e.g., ileal conduit, enteric bladder reconstruction)
Immunodeficiency
Renal transplant
Children
High-risk occupations (e.g., pilots)
Multiple stones

pneumonia, and gynecological conditions such as ectopic pregnancy, salpingitis, tubo-ovarian abscess, and torted ovarian cyst.

5. The use of imaging is increasing, and a growing number of patients are likely to be diagnosed with an incidentally identified renal calculus. The best management strategy for asymptomatic renal stones is unknown. At present no consensus exists as to which of these patients should be actively treated and which patients will pass stones spontaneously or will require intervention. Outcomes in studies looking at the natural history of asymptomatic stones <10 mm in diameter include a symptomatic stone event (13–32 %), spontaneous stone passage (13–20 %), size increase (30–46 %), and intervention (7–26 %). Certainly stones located within the renal pelvis or stones >15 mm in diameter are at high risk of progression (increase in size, symptomatic event, or need for intervention). One retrospective study of asymptomatic stones kept under observation showed that renal stones >4 mm were 26 % more likely to progress than those <4 mm ($P = 0.012$). Thus, asymptomatic renal stones of >5 mm in diameter or lying within the renal pelvis should be referred for a urological opinion.
6. For the purpose of this chapter, we have termed certain patient characteristics as red flags, with these patients warranting mandatory urological referral. Some of these patient-related factors can identify patients at high risk of stone progression (e.g., solitary kidney), while others may suggest alternative diagnoses (e.g., hydronephrosis). A list of red flags is reported in Table 22.3.
7. Once a patient has been deemed suitable for surveillance, then an appropriate follow-up method must be chosen. Again no guidelines exist for the optimum modality and frequency of imaging in this situation. The goals of serial imaging are to identify increase in stone size, change in location, stone passage, or hydronephrosis. While low-dose noncontrast CT is the gold standard for diagnosing urinary tract stones, it is not available in primary care and is not appropriate for stone surveillance given the concerns over repeated exposure to ionizing radiation. If a stone is radiopaque, then we recommend an annual KUB X-ray, along with measurement of renal function and urinalysis. If it is radiolucent, then we suggest substituting X-ray with KUB ultrasound, ideally carried out in the stone

clinic. If there has been no stone progression over 3 years, then it is appropriate to discontinue surveillance and repeat imaging only on the basis of new symptoms.

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Chapter 23
Renal Mass

Paolo Gontero

Abstract Any enlargement of the kidney can be defined as a renal mass. Several benign and malignant conditions present with a renal mass. Due to the retroperitoneal location of the kidney, a renal mass may grow as big as a watermelon, even producing a visible deformity of the abdomen, with little or no bother for the patient. Such a clinical presentation is nowadays less frequent due to the widespread use of ultrasound. As a result, most renal masses, chiefly the malignant ones, are diagnosed at an early stage when they are smaller and asymptomatic. A solid renal mass has to be considered as a malignant tumor until otherwise proven and thus needs a urological referral. Hydronephrosis is a common cause of renal mass that can be due to a variety of clinical conditions, either malignant or not. While all cases of hydronephrosis will eventually require a urological referral, the degree of urgency largely depends upon the underlying disease that can be better elucidated by a contrast CT. Benign conditions such us renal cysts are usually well characterized by a kidney ultrasound. Specialist referral depends upon symptoms and size. The aim of this chapter is to provide the GP with a working algorithm to manage a patient that either is found to have a palpable renal mass or is frightened by the occasional finding of a renal mass during a routine ultrasound.

Keywords Renal mass • Hydronephrosis • Kidney cancer • Renal cyst • Angiomyolipoma • Urological referral

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Introduction

We use the term renal mass to indicate any increase in size of the kidney whatever the condition or underlying disease. Several benign and malignant conditions present with a renal mass. Due to the retroperitoneal location of the kidney, a renal mass may grow as big as a watermelon, even producing a visible deformity of the abdomen, with little or no bother for the patient. Such a clinical presentation is nowadays less frequent due to the widespread use of ultrasound. As a result, most renal masses, chiefly the malignant ones, are diagnosed at an early stage when they are smaller and asymptomatic.

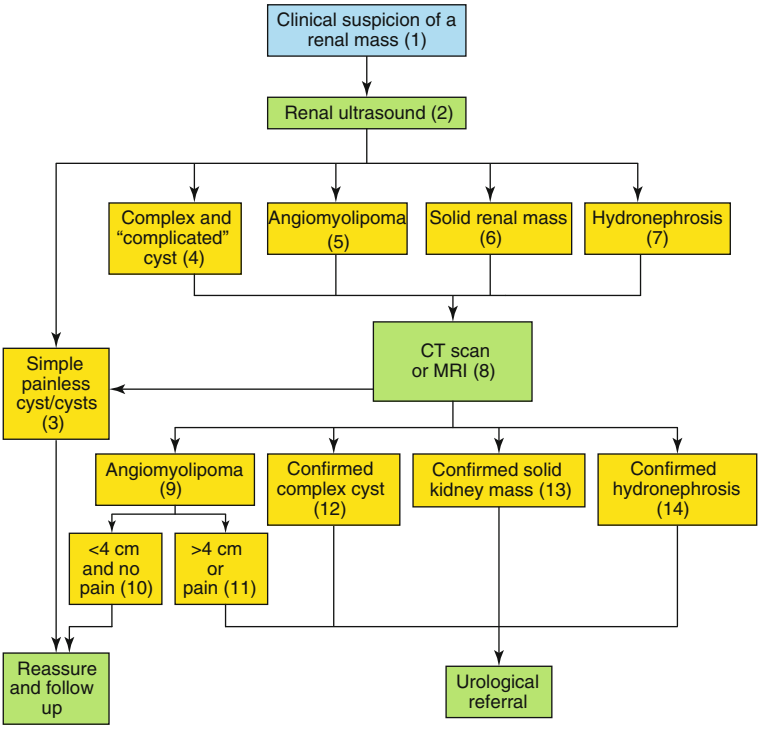
Not all renal masses, particularly those that possess clear benign features, necessarily need a urological referral. Rather, they can be effectively managed by the GP. Not all malignant renal masses represent a urological emergency as most small kidney cancers observed in active surveillance protocols tend to have a relative indolent behavior. Conveying this information to the patient may help to reduce the panic while waiting for the urological appointment.

The aim of this chapter is to provide a practical algorithm to make a differential diagnosis among the most common etiologies of a renal mass and to provide basic information for the work-up of those that can be managed by the GP.

Basic Investigation and Management of a Renal Mass

Comments About Flowchart 23.1

1. Suspicion for a kidney mass may raise from a palpable mass or from the patients' complaint of a discomfort in the loin.
2. A renal ultrasound (US) represents the first-line investigation in these cases. It is easily accessible and cost effective and has a high sensitivity in discerning between benign cystic lesions and solid masses with a high propensity to be malignant.
3. Any cystic lesion with a pure anechoic content and a thin, regular wall will be described by the radiologist as a "simple cyst." This description means the lesion has to be considered benign. Simple cysts may greatly vary in size (from few millimeters up to a football ball) and number (solitary or multiple). As far as the location is concerned, simple cysts are usually superficial, thus protruding outside the contour of the kidney. Some are deeply located in the kidney with the cystic wall in close contact with calices and the pelvis, hence the name of "parapelvic" cysts. It is still debatable whether the origin of simple cysts is congenital or acquired. Simple cysts are easily distinguished by uncommon conditions such as the *multicystic kidney of the newborn* (a nonhereditary, unilateral, malformation where the kidney is transformed in a nonfunctioning mass of cysts, often associated with other malformation of the contralateral upper urinary tract) and the *adult polycystic kidney disease*. This latter condition is an autosomal dominant hereditary condition, bilateral in 95 % of cases, with enlarged kidneys studded with multiple cysts that can often evolve into end-stage chronic renal failure in middle or advanced age.



Flowchart 23.1 Management of a renal mass

Simple cysts can grow over time, but if they remain asymptomatic or maintain the anechoic content with a regular thin wall, no further investigation but just US follow-up is all that is required for a simple cyst. Up to 10 cm in size, most of the simple cysts will be asymptomatic. As the cyst grows, the renal parenchyma is compressed, but rarely this leads to impaired renal function. All cases of "complicated" cysts or "complex" cysts warrant further investigations (see point 4).

4. Any kidney cyst not falling in the US description of a pure anechoic content and a thin, regular wall has to be considered as a "complicated" or a "complex" cyst. Infection of the cyst or the presence of hemorrhagic fluid (this latter situation can be found in 5 % of all cysts and is often associated to papillary cancer on the cystic walls) gives rise to variable degrees of hyperechoic content at the US. Calcification of the wall and septa within the cysts often makes the US picture unclear. These conditions need careful consideration due to the risk of underlying cancer cells within the cyst. Finally simple cysts may be located in such a position to compress the ureter, causing progressive hydronephrosis (see point 7). Any US appearance of a "complicated" or "complex" cyst needs to be further investigated, chiefly with a CT scan (see point 8). Notably, hydronephrosis itself may be confused with multiple parapelvic cysts and further investigations (CT scan) may be warranted in order to avoid this misdiagnosis.

5. Angiomyolipoma is a relatively rare benign tumor of the kidney. It is considered a renal hamartoma sometimes associated to a familiar inherited disorder named tuberous sclerosis. It can be solitary or multiple and of variable size. It is characterized by three benign histologic components: mature fat cells, smooth muscle, and blood vessels. US can easily recognize fat in this lesion and thus it is quite accurate in the diagnosis of an angiomyolipoma. If the radiologist is not absolutely sure of the diagnosis of angiomyolipoma, a contrast CT should be carried out.
6. US is usually highly sensitive in detecting a solid renal mass which has to be considered as malignant until otherwise proven. As a consequence, any diagnosis of a solid renal mass on US should prompt further investigation, essentially a contrast CT.
7. Hydronephrosis, that is, a dilatation of the pelvis and the calices usually due to an obstruction of the urinary collecting system (located in the ureter or lower urinary tract), can occasionally enlarge the kidney at such an extent to present with a palpable mass. The underlying disease can act with an acute mechanism (usually accompanied by pain in the form of a renal colic [see Chap. 1) or with a chronic mechanism (that can have a relatively painless course). Hydronephrosis causes progressive loss of kidney function. Moreover, a number of malignant diseases can be implicated in the etiology of hydronephrosis (Table 23.1). For this reason any finding of hydronephrosis warrants prompt identification of the underlying disease and its treatment. While a US can easily identify even mild degrees of hydronephrosis, only in a minority of cases can it detect the underlying disease due to its inability to accurately explore the ureter. Additionally, US is unable to provide any direct information on the degree of kidney impairment. A contrast CT is thus an essential diagnostic step in all cases of hydronephrosis where US has failed to provide an accurate diagnosis; it also provides essential information on the degree of kidney impairment.
8. Any diagnostic doubt with US warrants a contrast CT scan. Multiphase imaging CT scan is crucial to optimize diagnosis of a kidney mass. This means that the kidney needs to be observed not only in the early phase following injection of contrast (when the contrast is in the glomeruli) or in the nephrogenic phase when it is in the tubules and interstitium but also in the urographic phase (so-called URO-CT), when it is excreted in the pelvis. Multidetector helical CT scanners allow the generation of high-quality three-dimensional and multiplanar images with increased diagnostic ability in identifying the nature of a kidney mass. Some patients are allergic to iodinated contrast media employed during CT. Additionally, iodinated contrast media are usually contraindicated in patients with impaired renal function. In such cases, magnetic resonance imaging (MRI) can represent a reasonable and effective alternative to investigate a renal mass. While MRI without contrast can provide some information on the upper urinary tract, kidney vascularity, and nature of renal masses, contrast enhancement with gadolinium (a contrast medium better tolerated in case of impaired renal function) is needed for optimal assessment of anatomy and function of the kidney. MRI should be viewed more as an alternative to CT when the latter is contraindicated rather than a complementary investigation in the assessment of a renal mass.

Table 23.1 Common causes of hydronephrosis

Mechanism	Location	Disease	Suggestive clinical features	Laterality
Obstructive	Upper urinary tract	Ureteral tumor	Hematuria, risk factors (smoking), history of bladder cancer	Monolateral
		Stone	History of renal colic, rarely painless, hematuria	Usually monolateral
		Pelvic ureteral obstruction	Usually congenital, early (antenatal) diagnosis nowadays, usually painless	Mostly unilateral
		Retroperitoneal tumor (lymphoma)		Bilateral or unilateral
		Retroperitoneal fibrosis (idiopathic or acquired following radiotherapy)	Previous radiotherapy	Usually bilateral
		Iatrogenic ureteral injury	Previous abdominal surgery	Monolateral
		Vascular (aneurysm)	Atherogenic risk factors, abnormal aortic pulsation	Monolateral
		Ureteral endometriosis	Young women	Monolateral
		Bowel inflammatory diseases (Crohn disease, appendicitis abscess)	Abdominal pain	Monolateral
	Lower urinary tract	Bladder tumor at the ureteral orifices	Hematuria, smoking	Unilateral or bilateral
		Advanced prostate cancer	Hard-feeling prostate, high PSA	Unilateral or bilateral
		Cervix/uterine cancer	Pelvic mass on vaginal examination	Bilateral (can be unilateral)
		Chronic urine retention due to severe obstructive uropathy, neurogenic bladder	Palpable bladder, LUTS	Mostly bilateral
Nonobstructive		Vesicoureteral reflux	Recurrent urinary tract infections, pediatric age	Usually bilateral
		Functional (high fluid intake)	Usually subsides after bladder voiding	bilateral

9. Both CT and MRI can easily diagnose an angiomyolipoma due to the high fat content. Less than 5 % of angiomyolipomas do not contain fat and represent a diagnostic challenge. The management of angiomyolipomas depends on their risk of rupture causing retroperitoneal bleeding and whether they are symptomatic or not.
10. Since the risk of rupture is minimal for angiomyolipomas less than 4 cm in size, annual follow-up with US or CT is sufficient if there are no symptoms.
11. Angiomyolipomas exceeding 4 cm or accompanied by symptoms should be referred to the urologist. In these cases, selective arterial embolization is the preferred treatment option.
12. When the finding of a complex cyst is not clarified by a CT or by an MRI, the patients should be sent for a urological referral as a kidney cancer has to be excluded. The Bosniak classification of simple renal cysts is an aid to determining the chance of malignancy based on imaging criteria. Type I cysts are simple and smooth walled, with clear fluid; type II are also benign but may have minimal septations and a small fine rim of calcification; type III are more complex, with more calcification, increasing septations, and a thick cyst wall; and type IV have a thickened irregular wall, often with calcifications, and a mass may be noted inside the cyst, suggesting carcinoma. Numerous variations of the findings are used as a guide in the diagnosis of renal cancer. Any confirmed complex cyst or cysts that fall in the Bosniak II to IV classification on CT and/or MRI need a urological referral.
13. Any confirmed solid kidney mass at CT has to be considered a kidney malignant tumor until otherwise proven. The majority of them (more than 80 % of all malignant kidney tumors) will turn out to be renal cell carcinomas (RCC). Up to 35 % of patients with a RCC will eventually die of the disease. A urological referral is thus mandatory. However, a non-insignificant proportion of solid kidney masses, when of small size (3 cm or less), will eventually turn out to be benign. Hence, the expanding role of kidney biopsy in recent years, a procedure that nowadays can be performed as outpatient, should be viewed as a valuable and safe diagnostic tool. The prognosis of a malignant kidney tumor largely depends on its stage and the TNM staging system is currently the most valuable tool to define the aggressiveness of the disease. The prognosis is considered generally excellent (90 % 5-year survival) for RCC that are confined to the kidney (stage T1 or T2 disease) but it becomes less favorable for tumors invading structures surrounding the kidney (T3 or T4 disease, 30–50 % survival at 5 years) and gives little or no chance of cure in case of metastatic spread (which still occurs in 30 % of newly diagnosed RCC). Surgical ablation is the mainstay treatment option for RCC. Nonetheless, small (<4 cm) renal tumors confined to the kidney have shown a relatively indolent course when followed up without treatment, making the role of active surveillance a feasible option for elderly or comorbid patients at high risk for surgery. While RCCs confined to the kidney (stages T1 and T2) or not invading beyond the perirenal fat have a high chance of cure with surgery alone, kidney tumors that invade adjacent organs (T4) or the lymph nodes (N+) are at high risk of dying the disease even after surgery and need additional medical treatment (immunotherapy or biological oral agents).

Table 23.2 Treatment options and prognosis of renal cell carcinoma (RCC) by pathologic stage as defined by TNM

TNM stage	Explanation of TNM	Treatment options	5-year probability of survival (%)
T1 or T2 stage	Tumor confined to the kidney	1. Surgery (radical or partial nephrectomy): standard of care 2. Ablative therapies (cryotherapy or radiofrequency): <4 cm tumors, high surgical risk patients 3. Active surveillance: elderly and comorbid patients	80–90
T3 stage	Tumor invading the perirenal fat or the renal vein (T3a) or the vena cava (T3b)	Surgery (radical nephrectomy with or without removal of the neoplastic thrombus)	50
T4 stage and/or N+ disease	Tumor invading adjacent organs and/or the lymph nodes	Surgery + systemic therapy	20
M+ disease	Tumor with distant metastases	Systemic therapy	0 (median survival 5–36 months)

RCC with systemic metastases (M+) are usually candidates only for palliative systemic treatment as the benefit of surgery is minimal. Table 23.2 summarizes some therapeutic and prognostic information according to the stage of RCC.

14. Upon confirmation with a contrast CT scan, any case of hydronephrosis warrants a urological referral. When a neoplastic disease has been demonstrated or is highly suspected, the referral should be urgent. Similarly, acute obstructions due to stones need an urgent referral since irreversible kidney function damages may occur within 3 weeks. For asymptomatic long-standing hydronephroses due to congenital diseases or nonfunctioning kidneys due to benign conditions, a urological appointment can be made without urgency.

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Part III
Decision Making Based on Laboratory Abnormalities

Chapter 24
Raised Prostate-Specific Antigen

Roger S. Kirby

Abstract Prostate-specific antigen (PSA) may be raised as a result of prostate cancer, benign prostatic hyperplasia (BPH), or prostatic infection. The European randomized study of PSA screening confirmed that prostate cancer mortality could be reduced by the measurement of PSA. A raised PSA usually prompts a transrectal ultrasound (TRUS)-guided biopsy. If this is positive, other staging investigations are indicated, including magnetic resonance imaging (MRI) and a bone scan. With all of this information to hand, an informed decision has to be made about which treatment option is best for that individual.

Keywords Prostate-specific antigen • Prostate cancer

Introduction

A raised prostate-specific antigen (PSA) is one of the most common indications for referral to a urologist. However, before a PSA test is undertaken, it is important that a frank and honest discussion should be had with the patient about the pros and cons of this blood test. PSA determination should be seriously considered for all men with a life expectancy of 10 years or more, for whom identification of prostate cancer could potentially increase life expectancy. A recent European screening study has confirmed that a PSA screening test can reduce the risks of dying of prostate cancer by 21 %. It should be appreciated though that it is often not possible, however, to distinguish men with prostate cancer from those with BPH on the basis of a single PSA measurement; a transrectal ultrasound-guided prostatic biopsy is usually required, and patients should be informed of this, together with a discussion

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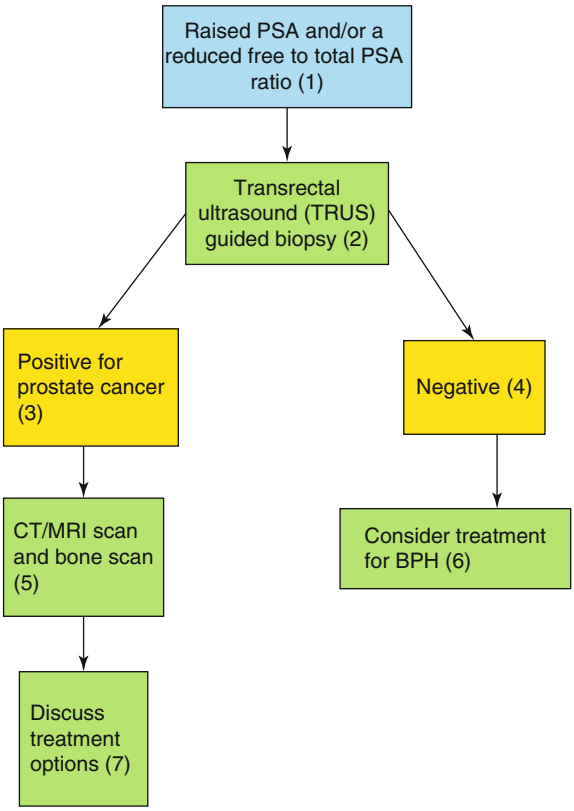
about the other uncertainties surrounding the optimum treatment for any prostate cancer discovered. A digital rectal examination (DRE) should already have been performed. This may reveal a symmetrically enlarged prostate, suggesting benign prostatic hyperplasia, or asymmetry, with a palpable nodule that would raise the suspicion of an adenocarcinoma.

Measurement of PSA increases the likelihood of detecting prostate cancer over and above digital rectal examination (DRE) alone and is most relevant, therefore, in such men, who are most likely to benefit. Overall, if PSA levels are above the upper limit of normal (i.e., 4.0 ng/mL), the likelihood of prostate cancer being present on biopsy is about 20–25 %. If PSA is considerably elevated (>10 ng/mL), the likelihood of cancer rises to over 50 %. In general, the higher the PSA, the greater the chance of prostatic malignancy being present on biopsy. It has also become apparent that in the absence of prostate cancer, measurement of serum PSA values can provide a useful indication of overall prostate volume. This, in turn, can predict those patients most likely to suffer BPH progression and facilitate the selection of agents for medical therapy of BPH. Not surprisingly, men with enlarged prostates and high PSA values (arbitrarily set as volume >30 cm^3 and PSA value >1.4 ng/mL) appear to benefit most from 5α-reductase inhibitors, which act primarily by reducing the prostate volume.

It has been also been reported that PSA in the circulation exists in two forms: a "bound" form, which is complexed to one of two proteins – either antichymotrypsin or α_2-macroglobulin – and a "free" or uncomplexed form. For reasons that are not fully understood, the ratio of free to total PSA declines in patients harboring prostate malignancy. Moreover, the more biologically aggressive the tumor appears to be, the greater the reduction in the free to total PSA ratio. Patients with a total PSA level above 4.0 ng/mL and a free to total PSA ratio below 0.18 should usually be referred to a urologist and considered for prostatic biopsy.

Comments About Flowchart 24.1

1. A raised PSA is usually regarded as a serum PSA greater than 4.0 ng/mL. As PSA values have been shown to rise as men grow older, some practitioners advocate age-adjusted PSA cut points. PSA values are also greater in men with a larger prostate, which has led to the concept of PSA density. PSA exists in both free and bound forms in the circulation. A free to total PSA ratio of less than 0.18 has been shown to be associated with a greater risk of that person harboring a cancer within the prostate.
2. Transrectal ultrasound (TRUS) biopsy is still the most commonly employed method of obtaining tissue from the prostate for histological analysis, thereby establishing the diagnosis of prostate cancer. The technique requires the administration of prophylactic antibiotics (usually the aminoquinolone ciprofloxacin) in combination with gentamicin to reduce the risk of post biopsy sepsis. A lubricated ultrasound probe is inserted into the rectum and the biopsy needle channel used to infiltrate the prostate with local anesthetic. From 12 to 20 targeted cores of prostate tissue are then taken using an automated biopsy device. These are sent for histological examination. Of late there has been a move towards trans-perineal biopsy of the prostate as there is a substantially lower risk of infection. However, there is a higher incidence of post biopsy urinary retention after this procedure.



Flowchart 24.1 Management of raised PSA

3. If the histopathological analysis proves positive for prostate cancer, a Gleason score will be attributed to each focus of cancer. The Gleason system assigns a number from 1 to 5 to the cancer; the greater the number, the more aggressive the cancer is considered to be. Because prostate cancer is rather heterogeneous pathologically, the primary pattern (i.e., 4) is added to the secondary pattern (i.e., 3) and the two patterns summated and expressed as $4+3=7$ formula. In practice only Gleason pattern 6 (well differentiated), Gleason pattern 7 (moderately well differentiated), and Gleason 8–10 (poorly differentiated) cancers are encountered in clinical practice. The percentage of each core involved by tumor is also used to estimate the volume of the prostate involved by cancer. The presence or absence of perineural invasion is also commented on although in practice this does not change the management.
4. If the histopathological analysis proves negative for cancer, then the prostate is most likely to be affected by benign prostatic hyperplasia (BPH). Although urinary tract infections (UTIs) and prostatitis can sometimes be associated with an elevated PSA. In the absence of cancer the PSA value can be used as a surrogate for prostate volume and is also of value in selecting which form of medical therapy to employ.

5. When the prostate biopsies are positive for prostate cancer, further staging investigations are often indicated. Magnetic resonance imaging (MRI) is ideally delayed for 6–8 weeks after the biopsy because of the distortion of the image caused by biopsy artifact. New 3 Tesla technology with gadolinium enhancement is currently improving the quality of the images obtained and therefore providing a better estimate of the volume and location of the tumor within the prostate and the risks of involvement and penetration of the capsule of the gland. MRI is also used to evaluate the risk of lymph node spread of the tumor and may sometimes reveal metastases within the bony pelvis or lumbar spine. A radionuclide bone scan is indicated if the PSA > 10 mg/mL or there are specific symptoms of back pain or other skeletal symptoms.
6. If the patient is inconvenienced by lower urinary tract symptoms (LUTS) of frequency and poor flow, then medical treatment with either an alpha-blocker, a 5-alpha reductase inhibitor (5-ARI), or a combination of the two may be indicated. If the PSA value is less than 1.4 ng/mL, then the prostate is generally small and unlikely to respond to the prostate shrinking effect of a 5-ARI such as dutasteride. Instead, an alpha-blocker such as tamsulosin should be prescribed. In men with a larger prostate (>40 ccs) and a PSA > 1.4 ng/mL, treatment with a 5-ARI has been shown to reduce the risk of BPH progression to acute urinary retention (AUR) and the need for surgery. Men with a larger prostate and bothersome LUTS are best managed with combination therapy of an alpha-blocker and a 5-ARI.
7. Treatment options for men with prostate biopsies positive for adenocarcinoma will vary according to the grade and stage of the cancer. When only a minority of the cores are involved with low-risk Gleason pattern 6 prostate cancer, many men are managed in an active surveillance (AS) protocol with 3 monthly PSA measurements and a repeat MRI and prostate biopsy at 1 year. Current data suggest that only around one-third of these men will go onto require definitive treatment. If moderately differentiated, moderate-risk Gleason pattern 7 cancer is present, most urologists advocate therapy with curative intent. Treatment options include surgery (open, laparoscopic, or robotic), radiotherapy (external beam or brachytherapy), cryotherapy, and high-intensity focused ultrasound (HIFU). For patients with locally advanced prostate cancer, most authorities recommend external beam radiotherapy with hormonal downstaging. Androgen ablation therapy is often continued for up to 2 years after completion of the radiotherapy. For men with metastatic prostate cancer, hormonal therapy is standard, usually with luteinizing hormone-releasing hormone (LHRH) analogues. Second-line treatments with Taxotere, Cabazitaxel and Abiraterone are now available and are extending survival statistics in men with hormone-escaped prostate cancer.

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Chapter 25
Raised Serum Creatinine/Reduced Estimated Glomerular Filtrate

Robin G. Woolfson

Abstract The finding of an elevated creatinine level may be the first sign of chronic kidney disease. This affects 10 % of the population, usually occurring in the context of chronic disease such as diabetes mellitus, hypertension, systemic atherosclerosis, and heart failure which accounts for 95 % of patients. This chapter provides a pathway to evaluate the significance of an elevated creatinine and is directed towards doctors working in both primary and secondary care.

Keywords Creatinine • eGFR (estimated glomerular filtration rate) • CKD (chronic kidney disease) • Proteinuria • Albuminuria

Introduction

Creatinine is a breakdown product of creatine phosphate in muscle cells with the quantity generated dependent on muscle mass, which reflects age, gender, and ethnicity. With a small proportion secreted by the proximal tubule, most creatinine is excreted by glomerular filtration and is therefore used as a measure of renal function. Serum creatinine levels are affected by recent dietary intake of meat, dehydration, drugs which block the angiotensin II pathway, diuretics, NSAIDs, and drugs such as trimethoprim, cimetidine, and certain antiarrhythmics which inhibit tubular secretion of creatinine. The finding of a raised serum creatinine must prompt a repeat test to confirm a persistent abnormality.

Formulae are used to convert creatinine levels into estimated glomerular filtration rate (eGFR). In the UK, the modification of diet in renal disease (MDRD) formula is used because it includes a correction factor for Black patients (African-Caribbean or sub-Saharan African) amongst whom chronic kidney disease is six times more prevalent.

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Table 25.1 Stages of chronic kidney disease (CKD)

Stage[a]	GFR (ml/min)	Description
1	³ 90	Not CKD unless presence of proteinuria, microscopic hematuria, abnormal imaging, or abnormal renal biopsy
2	60–89	
3A	45–59	Moderate decrease in GFR. Most patients with CKD stage 3A have age-related nephropathy rather than progressive disease
3B	30–44	
4	15–29	Severe decrease in GFR, with or without other evidence of kidney damage
5	<15	Established renal failure

[a]Use suffix (p) to denote presence of proteinuria (ACR > 30 mg/mmol) when staging CKD

Table 25.2 Risk factors for chronic kidney disease

Diabetes mellitus
Hypertension
Cardiovascular disease including heart failure and coronary, cerebral, and peripheral vascular disease
Structural renal tract disease including reflux nephropathy, childhood urosepsis, and renal calculi
Bladder outflow tract obstruction, due to prostatic hypertrophy, urethral strictures, and dyssynergia
New nocturia, urgency, hesitation, reduced urinary stream, nocturnal enuresis, or infection
Multisystem diseases, e.g., systemic lupus erythematosus, vasculitis, rheumatoid arthritis, multiple myeloma
Detection of proteinuria with or without hematuria
Chronic use of nonsteroidal anti-inflammatory drugs (NSAIDs) or certain alternative remedies, including Chinese herbs
Black or Asian ethnicity
Family history of stage 5 CKD or hereditary kidney disease

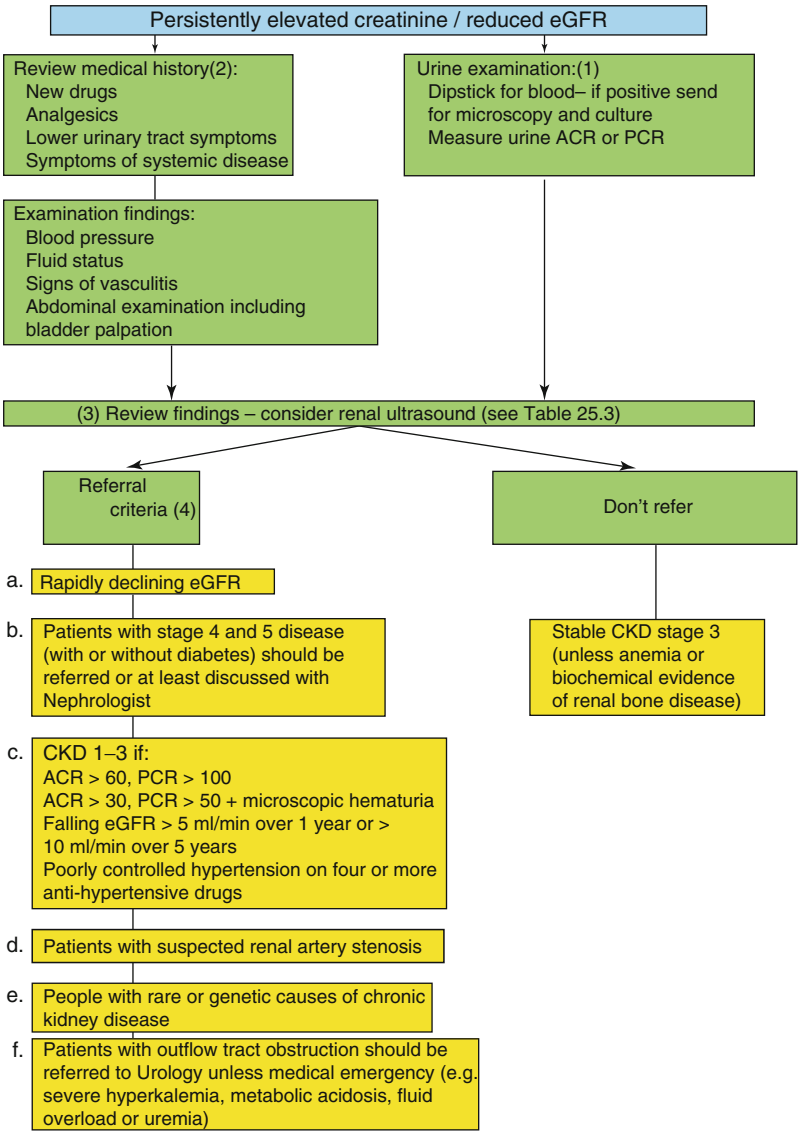
The eGFR is useful but does not take into account the muscularity of any given individual and will therefore underestimate the renal function of individuals with above average musculature and overestimate renal function for those with below average musculature. In the absence of proteinuria, hematuria, and abnormal imaging, a corrected eGFR of 60 ml/min or more reflects normal function. eGFR levels are no more accurate than the creatinine level from which they are calculated, so abnormal results must be repeated. Chronic kidney disease (CKD) is divided into five stages depending on eGFR and the presence of proteinuria (see Table 25.1).

CKD affects 10 % of the population, usually occurring in the context of chronic disease such as diabetes mellitus, hypertension, systemic atherosclerosis, and heart failure which will account for 95 % of cases. Other patient groups at risk of CKD are listed in Table 25.2.

Basic Investigation and Management of Raised Serum Creatinine

Comments About Flowchart 25.1

1. If a creatinine level is found to be newly elevated, then repeat within 2 weeks and check urine dipstick for blood, sending urine sample to measure albumin/creatinine ratio (ACR) or protein/creatinine ratio (PCR).



Flowchart 25.1 Persistently elevated creatinine/reduced eGFR

2. Review medical history for relevant chronic disease (see Table 25.2), medication (both newly prescribed and over the counter which may adversely affect glomerular filtration or tubular secretion of creatinine), urinary symptoms, and symptoms of systemic disease. Review family history. See Table 25.2.
3. Consider need for renal referral and ultrasound (see Table 25.3).
4. Referral to a nephrologist is mandatory in any patient with persistently elevated creatinine/reduced eGFR and at least one of the clinical situations reported in boxes a–f.

Table 25.3 Indication for kidney and bladder ultrasound

Progressive CKD
Visible or persistent invisible hematuria
Lower urinary tract symptoms
Family history of polycystic kidney disease and are aged over 20
Stage 4 or 5 CKD
Patients who will require a renal biopsy

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Chapter 26
Microscopic (Non-visible) Hematuria

Paolo Gontero

Abstract Microscopic hematuria is detected during a urine dipstick or an examination of the urine sediment. It is conventionally defined as the presence of three or more red blood cells per high-power field in the sediment or at least "1+" of blood at urine dipstick. There is no reason not to believe that any disease causing a gross hematuria may instead present exclusively with a non-visible hematuria. Thus, a microscopic hematuria should, in principle, deserve the same attention of a gross hematuria. The problem arises when looking at the prevalence of an asymptomatic microscopic hematuria. This finding can be found in up to 20 % of the population and in up to 70 % of cases remains without explanation even after an accurate work-up. It is clear that not all patients with microscopic hematuria need to be investigated. The aim of this chapter is to help the GP in the selection of those patients with microscopic hematuria deserving a diagnostic work-up and to guide him through the choice of appropriate specialist referral.

Keywords Hematuria • Microscopic • Significant • Persistent • High-risk patient • Low-risk patient

Introduction

Non-visible hematuria is usually detected in the urine sediment or a urine dipstick. There is no reason not to believe that any disease causing a gross hematuria may instead present exclusively with a non-visible hematuria. Thus, a microscopic hematuria

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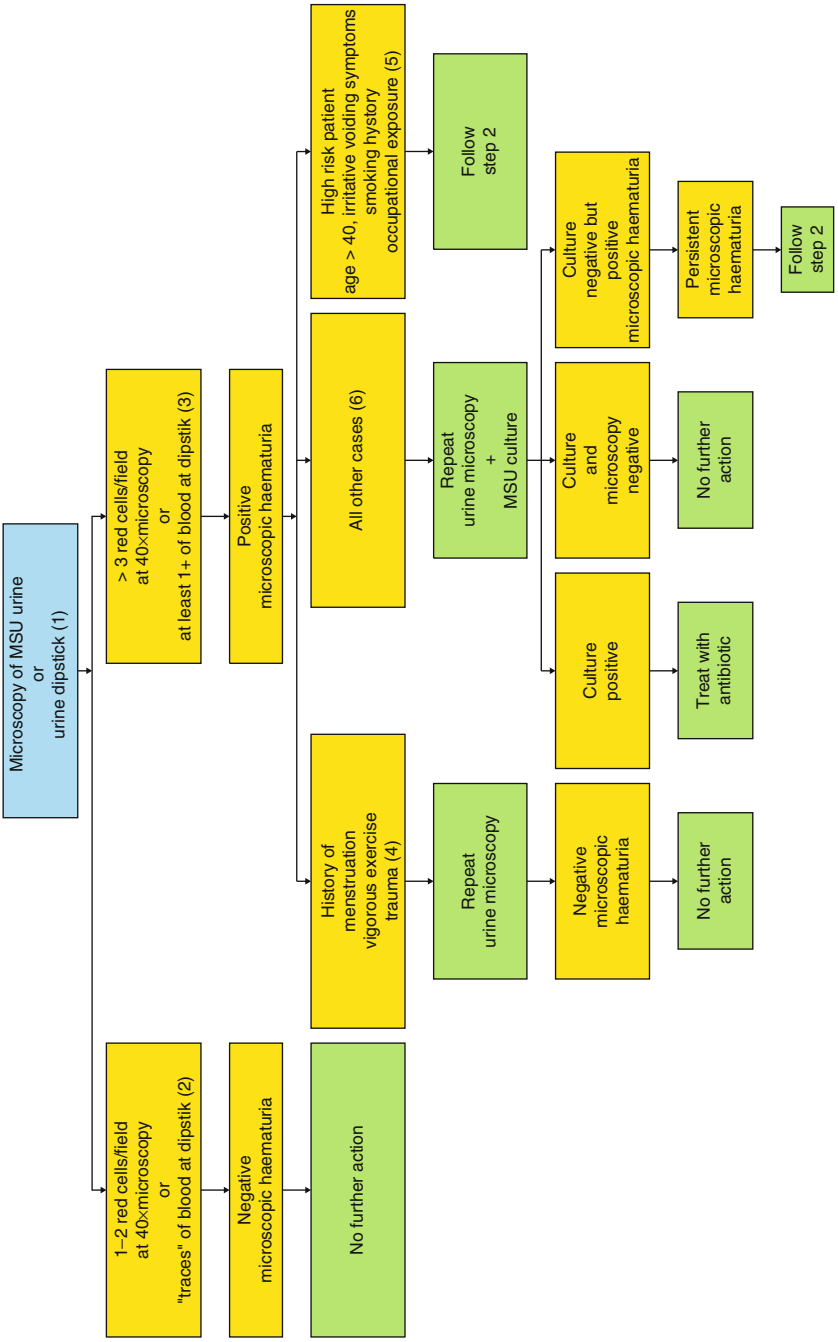
should, in principle, deserve the same attention of a gross hematuria (see Chapter 9). The problem arises when looking at the prevalence of an asymptomatic microscopic hematuria. This finding can be found in up to 20 % of the population and in up to 70 % of cases remains without explanation even after an accurate work-up.

Not all patients with microscopic hematuria need to be investigated. The first step is to identify those patients whose microscopic hematuria is significant to deserve medical attention. The second step will identify essential investigations to guide appropriate specialist referral of significant microscopic hematuria.

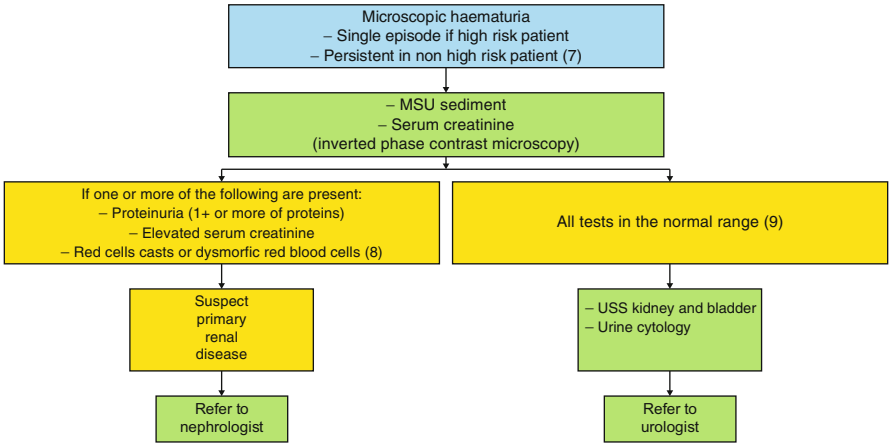
Step 1 Initial Evaluation: Which Patient Should Be Investigated?

Comments About Flowchart 26.1

1. Non-visible hematuria, named microscopic hematuria, can be occasionally found during a urine dipstick or an examination of the urine sediment. The first thing is to discriminate a true, significant microscopic hematuria from a non significant presence of blood.
2. The presence of *1–2 red blood cells per high-power field* (observed at 40×) in the sediment or "trace" hematuria at dipstick should be considered negative. No further action is indicated.
3. Significant hematuria is considered the presence of *3 or more red blood cells per high-power field* in the sediment or at least *1+ of blood* at urine dipstick. There is no distinction in significance between non-hemolyzed and hemolyzed dipstick-positive hematuria and thus 1+ for either should be considered of equal significance.
4. If the finding can be ascribed to menstruation, vigorous exercise, or a trauma of the genitourinary tract, then it is advisable to simply repeat the test after a few days, preferably a urine microscopy (sensitivity of a dipstick test for microscopic hematuria varies from 60 to 99 %). In case of normal finding, no further action is indicated.
5. The occurrence of microscopic hematuria, even at the first episode, in a patient considered at "high risk" for harboring a hematuria-related disease warrants further investigations. An age of over 40 years, smoking or occupational exposure to carcinogens (dye, rubber, or petrol industries), and the concomitant presence of irritative voiding symptoms (other than those easily attributable to a urinary tract infection) meet the definition of "high-risk microscopic hematuria" and prompt to follow the algorithm described in step 2.
6. For all the remaining patients (those not falling in the high-risk category and not fulfilling point 4), a repeat MSU microscopy with culture is recommended. Any proven urinary tract infection (UTI) should be treated with antibiotic. If microscopic hematuria is not confirmed, no further action is needed. Persistence of microscopic hematuria in the absence of UTI warrants application of the algorithm described in step 2.



Flowchart 26.1 Which patient with microscopic hematuria should be investigated



Flowchart 26.2 How to investigate and appropriately refer a patient with microscopic hematuria

Step 2 How to Investigate and Appropriately Refer a Patient with Microscopic Hematuria

Comments About Flowchart 26.2

7. High-risk patients with a single episode of microscopic hematuria or those with persistent microscopic hematuria (on repeated dipstick or urine microscopy) need specialist referral. Interpretation of some simple investigation results will guide appropriate referral. MSU microscopy and a serum creatinine may provide important hints to suspect a kidney problem.
8. A 1+ proteinuria at dipstick, an elevated serum creatinine (compared with the normal reference range), or red blood cells casts indicate the need of a nephrological referral. The presence of irregular-shaped red blood cells is also a sign of a nephrological origin of the hematuria. Unfortunately this finding is usually underreported in an MSU microscopy. Examination of the urine sediment through an inverted phase contrast microscopy is more reliable in the identification of the morphology of red blood cells and should be prescribed where possible.
9. If no abnormality suggestive of a renal disease is detected with the above-mentioned urine and serum tests, the patient needs a urological referral. It would be of help for the urologist to have the patient referred with a USS of the kidneys and the bladder and a urine cytology test. Similarly to a macroscopic hematuria, the most warring disease to be excluded in cases of microscopic hematuria of presumable urological origin is a cancer of the urinary tract (of the urothelium or of the renal parenchyma). The urologist will almost certainly recommend a cystoscopy besides more complex imaging of the upper urinary tract (Intravenous pyelogram (IVP) or contrast CT).

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Chapter 27
How to Interpret Findings of a Urine Cytology Test

Michael J. Bailey

Abstract Urine cytology is a laboratory test involving the microscopic examination of a spun deposit of a sample of voided urine.

One of the principle uses of urine cytology is to detect bladder cancer. While the test is very specific (a positive result indicates the presence of bladder cancer), it is not very sensitive (most patients with bladder cancer will not have positive cytology). Thus, while a positive result indicates the presence of bladder cancer, a negative result does not exclude the disease. Urine cytology is therefore not a viable test for population screening for bladder cancer.

In this chapter, the method of collection of urine samples, the indications for requesting urine cytology, and the interpretation of the results are discussed. An algorithm for action based on the results of a urine cytology test is presented.

It is emphasized that in cases where there are symptoms which could indicate the possibility of bladder cancer in a patient such as macroscopic painless hematuria, referral to a specialist should not be delayed while awaiting the results of a urine cytology test.

Keywords Urine cytology • VUC • Bladder cancer • Urothelial cancer • Tests for bladder cancer

Introduction: Definition of Urine Cytology

Urine cytology, commonly termed as voided urine cytology (VUC) is the microscopic examination of a urine sample, specifically looking for the presence of malignant cells therein. Other abnormalities such as red blood cells, presence of ova or parasites, bacteria, yeasts, or virus particles may also be seen and reported, but are not dealt with in this chapter.

The urine specimen is centrifuged, and the deposit stained and examined.

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When to Request a Urine Cytology Test

Urine cytology is not a good screening tool for the diagnosis or exclusion of bladder cancer. While the test is very accurate in detecting aggressive bladder cancer (true positive rate ~90 %), it is much less sensitive for the majority of bladder cancers which are either moderately or well differentiated (i.e., less aggressive) when the false-negative rate may be 60–70 %.

The use of urine cytology as a population screening tool cannot be recommended as the pickup rate is so low and the cost prohibitive. In a series of 1,000 consecutive patients with asymptomatic microscopic hematuria (i.e., already a group at risk of having bladder cancer), 660 urine cytology examinations were performed. Seventy-one patients were found to have urothelial cancer, but only 25 of these patients had positive cytology. A meta-analysis that included data on 18 published series with 1,255 patients reported a sensitivity for urine cytology of 34 % and specificity of 99 %.

However, urine cytology may be of value in assessing high-risk patients (risk factors = smoking, occupational exposure to carcinogens, age >50) or those with unexplained irritative symptoms.

Referral for a specialist opinion should not be delayed while waiting for a urine cytology result if there is a high suspicion of bladder cancer (e.g., painless macroscopic hematuria)

How to Perform the Test

Urine cytology can be performed on voided urine specimens voided urine cytology (VUC) or bladder washings – the latter almost always in a hospital setting.

In order to maximize the accuracy of the test, a voided urine specimen should be a midstream sample in a sterile container. It should not be the first void in the morning, as there will be a number of degenerate cells after overnight storage in the bladder. The specimen should be delivered to the laboratory for analysis as soon as possible and refrigerated if there is any delay. The request form should include as much clinical information as possible – especially important is to note if the sample is voided urine or has been collected by catheterization.

There is considerable interobserver variability in the accuracy of reporting, so a cytologist experienced in the interpretation of voided urine cytology (VUC) is recommended.

How to Interpret the Results

Test results are likely to be reported as negative (no malignant cells seen), positive (malignant cells definitely identified), or atypical (some abnormal cells, but not definitely malignant).

A positive result indicates the presence of a urothelial cancer, probably aggressive in nature and should prompt urgent urological referral. Non-urothelial malignant cells from an adenocarcinoma or squamous cell carcinoma in the urinary tract may also be seen occasionally and again require urgent specialist referral.

A negative result does *not* exclude bladder cancer – up to 70 % of patients with bladder cancer will have negative urine cytology – so if there are other reasons for referral to a urologist, a negative urine cytology does not mean that referral can be deferred.

An equivocal result or one specifying atypia may indicate a bladder tumor, usually of moderate or well-differentiated nature, but may also be the result of urothelial inflammation from another pathology such as infection or calculus disease. Again, a urological referral is appropriate if there are associated worrying symptoms, but if a urinary tract infection is suspected, repeat cytology after treating the infection may prove negative.

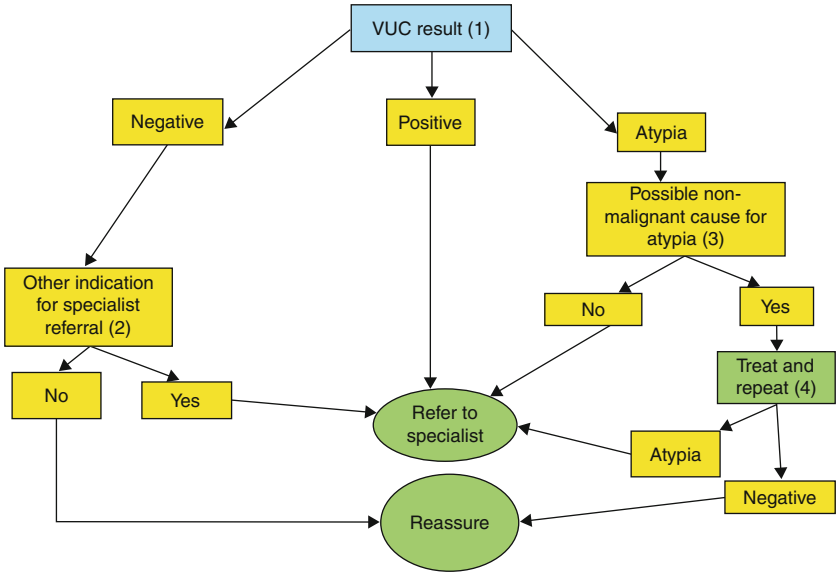
Use of voided urine cytology (VUC) in Follow-up of Patients with Known Bladder Cancer

While the role of voided urine cytology (VUC) in diagnosing urothelial carcinoma is limited, it can be useful in the follow-up of patients with known bladder cancer. Patients are routinely followed up with regular cystoscopy once their bladder cancer has been diagnosed and treated. The use of voided urine cytology (VUC) in between cystoscopies may give the patient and their doctor added reassurance that the tumor has not recurred. As with VUC in a diagnostic setting, positive results reliably indicate a poorly differentiated recurrence, but negative results do not exclude recurrence of a less aggressive nature. The combination of VUC and other urinary markers may at some point be able to reduce the frequency of cystoscopy, but tests are not yet sufficiently sensitive for this.

How to Manage a Patient Presenting with a voided urine cytology (VUC) Result

Comments About Flowchart 27.1

1. Test results of a patient presenting with a voided urine cytology (VUC) are likely to be reported as negative (no malignant cells seen), positive (malignant cells definitely identified), or atypical (some abnormal cells, but not definitely malignant).
2. In spite of a negative voided urine cytology (VUC), one or more of the following are indications for a specialist opinion: macroscopic painless hematuria, asymptomatic microscopic hematuria in the over 50s, unexplained irritative symptoms, and recurrent UTIs in older women.



Flowchart 27.1 Patient presenting with the results of a voided urine cytology (VUC)

3. Nonmalignant causes for atypia include recent UTI, urinary tract calculi, and recent urinary tract instrumentation (e.g., catheterization).
4. It is advisable to treat possible causes of atypia as described above and repeat the test after treatment. Leave 4–6 weeks for the urothelium to recover before repeating. Ensure that the urine sample is correctly produced, collected, and transported (see section "Introduction: Definition of Urine Cytology").

Conclusions

(VUC) should not be used as a population screening tool but targeted at the high-risk population.

With correct sample collection and an experienced cytopathologist, a positive result has a 95 % chance of indicating a urothelial cell carcinoma which will usually be within the bladder but may be in the upper tract.

A negative VUC does not exclude urothelial carcinoma, so specialist referral should still be made if the patient's symptoms warrant this.

VUC may be employed as part of the follow-up for patients treated for bladder cancer – this should be coordinated with the specialist undertaking cystoscopic follow-up.

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Chapter 28
Leukocytes in the Urine

Timothy Giles Nedas and Matthew Frank Bultitude

Abstract Leukocytes in the urine (pyuria) can be diagnosed either on dipstick testing or on microscopy. Leukocytes in the urine may be noted in conjunction with other findings on urinalysis or alone. They may also be noted in the presence or absence of urinary tract symptoms. This chapter will examine each situation in turn and try to provide you with management algorithms. Perhaps the most important consideration is that the presence of leukocytes in the urine does not always indicate the presence of urinary tract pathology.

Keywords Pyuria • Leukocytes • Urinary infection

Introduction

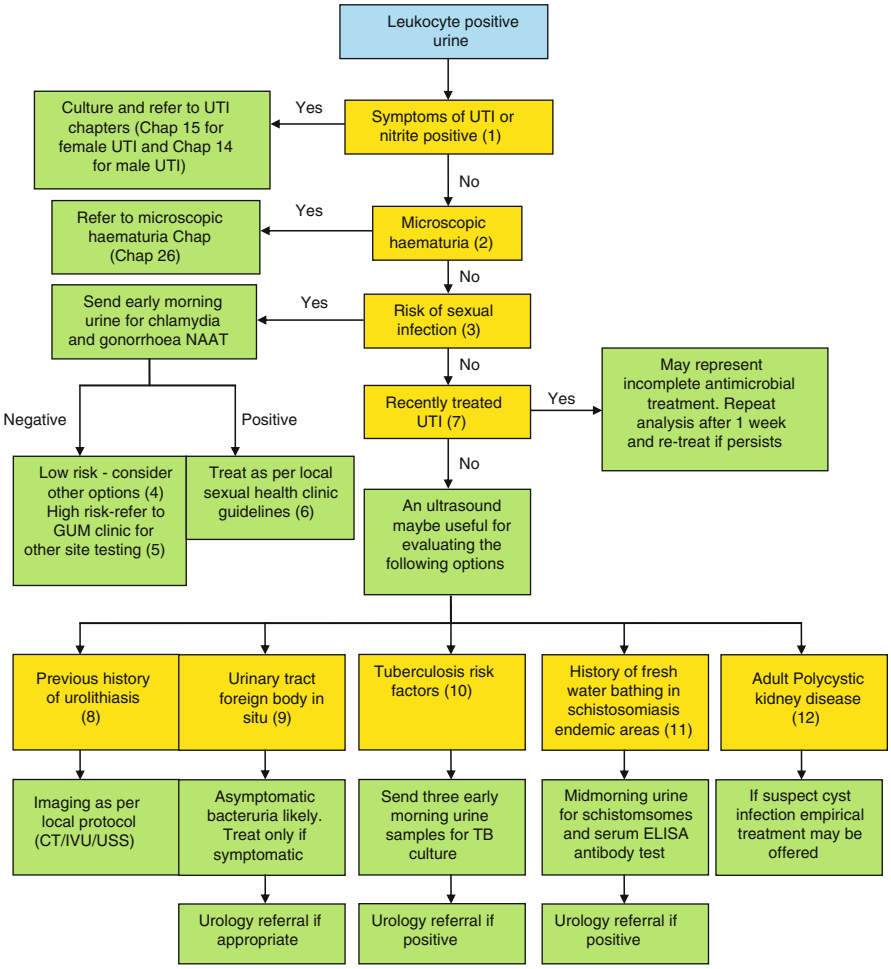
Leukocytes in the urine cause a change in color of the dipstick due to the action of the enzyme leukocyte esterase. On microscopy, >10 per high power field of centrifuged urine or per ml of fresh urine is required.

False-positive urine dipstick can result from contamination by vaginal discharge and the presence of formalin.

False-negative dipsticks can result from concentrated urine (high specific gravity), glycosuria, presence of urobilinogen, ingestion of large amounts of vitamin C, and too rapid or too delayed reading of the dipstick. If you note pyuria and send the urine off for culture, it is vital to note the European Association of Urology guidelines which clearly indicate "pyuria in the absence of signs or symptoms in a person with

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Flowchart 28.1 Leukocyte-positive urine

bacteriuria should not be interpreted as symptomatic of infection or as an indication for antimicrobial treatment."

Guidelines for the Management of Leukocyte-Positive Urine

Comments About Flowchart 28.1

1. Most bacteria in the urine reduce nitrate to nitrite, particularly Gram-negative organisms (e.g., *E. coli*), but the test may be negative if infection is caused by Gram-positive bacteria, *Pseudomonas aeruginosa* or *Enterococci*.

2. Microscopic hematuria may be a sign of nephrological or urological pathology. It may also be an isolated transient finding. Refer Chap. 26. It is worth reiterating that macroscopic/frank/visible hematuria always warrants urgent urological referral.
3. Gonorrhea and *Chlamydia trachomatis* are the two major sexual infections that may present with pyuria with Chlamydia being the most common curable sexual infection in Western countries. Although widespread asymptomatic testing is not advocated, gonorrhea may be asymptomatic in the female urethra, and pyuria along with a clinical risk would be a suitable indication. Nucleic acid amplification tests (NAAT) have become the preferred method of screening for gonorrhea and Chlamydia offering greater than 96 % sensitivity.
4. A negative NAAT test and low clinical risk means that sexual infection is unlikely and other causes for leukocytes in the urine should be evaluated. However absolute exclusion of nonspecific urethritis (nongonococcal non-chlamydial) can be established with a urethral smear.
5. High-risk patient groups are men who have sex with men, sex workers, postpubertal young patients, pregnant women, women who have had a hysterectomy, and known contacts of those with sexual health infections. These groups may benefit from a review in a sexual health clinic.
6. NAAT-positive patients should be treated for the appropriate organism according to local protocol.
7. Incomplete treatment of a urinary tract infection can result in the persistent presence of leukocytes in the urine. In this case further antimicrobial treatment may be offered.
8. Urinary tract stone disease recurs within 10 years in approximately 50 % of patients. It is worth arranging screening imaging investigations, such as urinary tract ultrasound (USS), intravenous pyelogram (IVP) or CT, for those patients with persistent pyuria and previous stone disease.
9. Urinary tract foreign bodies are most commonly urinary catheters, ureteric stents, or nephrostomy tubes. Catheters and nephrostomy tubes will frequently provoke bacterial colonization due to the connection between the atmosphere and urine. Leukocytes may be present as an isolated finding. Urinary tract stents post urological surgery will always result in the presence of leukocytes in the urine (along with protein and blood) and urinary tract symptoms. In practice there is rarely an infective process occurring rather than an inflammatory reaction in the presence of an iatrogenic foreign body. Symptomatic relief rather than empirical antibiotic treatment is recommended.
10. Tuberculosis (TB) of the urinary tract is caused by mycobacterium tuberculosis and accounts for 15–20 % of TB cases in developing countries. During primary infection of the lung there is early spread to the urinary tract and may present many years later as postprimary TB. Immunocompromise can precipitate this, e.g., HIV. The kidneys can develop granulomas causing caseous necrosis of the renal papillae. Eventually fibrosis and calcification lead to renal destruction. Spread from the kidney to the ureter can result in the development of ureteric strictures. The bladder can become ulcerated or tuberculous and here too, fibrosis can result in destruction. Genital tuberculosis frequently involves the epididymis in males or the prostate.

In the developed world the diagnosis of genitourinary TB is difficult due to its nonspecific symptoms, and the most important hints are patient's history and long latency of up to 30 years.

Investigations to diagnose TB of the urinary tract include at least three early morning urine specimens specifically cultured for TB. Urine culture for TB should be undertaken on Lowenstein Johnson medium and a pyruvic egg medium in order to detect any of the known strains of mycobacterium.

Urinary tract imaging should be undertaken as part of the investigations, which in the case of fulminant TB need only be a KUB radiograph and ultrasound, but in the early assessment should include a CT of the urinary tract and a cystoscopy.

Treatment of TB is as per local protocol but tends to involve 6 months of isoniazid and rifampicin. The management of urological consequences requires specialist assessment and preservation of urinary tract function with appropriate drainage or diversion.

11. Schistosomiasis, also known as bilharzia, is a parasitic disease caused by a trematode (fluke or flatworm) *Schistosoma haematobium*, and it affects more than 100 million people worldwide. It occurs commonly in Africa, Egypt, and the Middle East. Cercariae (the infective form of *S. haematobium*) are found in freshwater in endemic areas and enter humans by penetrating the skin. Adult flukes then mate in the liver. Fertilized eggs leave the infected patient by traversing blood vessels in the pelvis into the bladder (and also the rectum and sigmoid colon). These eggs then hatch in freshwater to grow into miracidia which are taken up by Bulinus snails (the intermediate host) where they produce further cercariae (by asexual multiplication) and thus the life cycle is repeated.

 An early sign of infection is Katayama fever or swimmers itch which is a localized itch accompanied by fever and sometimes a rash. Initial infection may however go unnoticed.

 Chronic exposure to the eggs (rather than the adult flukes which are well tolerated) can cause significant urinary tract problems including squamous cell bladder cancer. Investigations include a midday urine specimen examined for eggs (this is the time of peak egg output), a serum ELISA assay, and a cystoscopy which may show characteristic sandy patches in the bladder. Histological confirmation of bladder Schistosomiasis is the presence of eggs with terminal spines on bladder biopsy.

 The treatment of those with early Schistosomiasis is relatively straightforward being a single dose of praziquantel at 40 mg/kg or two doses at 20 mg/kg 4 h apart. Praziquantel disturbs the ionic exchange through the worms' membrane resulting in death. Metrifonate, an organophosphate that blocks the worm's cholinesterase enzyme, can also be used.

12. The only presenting sign of cyst infection in adult polycystic kidney disease may be persistent pyuria.

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Chapter 29
Bacteria in the Urine

Soumendra Nath Datta and Matthew Frank Bultitude

Abstract This chapter details the management of patients who are found to have bacteriuria on microscopy. Emphasis is placed on how to triage and manage these patients in primary care. Red flag findings are highlighted so that patients can be referred for imaging/admission. Asymptomatic bacteriuria, a common finding that only requires treatment in certain patient groups, is reviewed.

Keywords Asymptomatic bacteriuria • Culture • Urinary tract infection • Sepsis • Pregnancy • Children

Introduction

Urinary tract infection (UTI) is a common spectrum of clinical conditions ranging from simple cystitis to fulminant infection of the kidney with associated severe sepsis. Urine is normally sterile and the presence of bacteria may suggest a decrease in host defense mechanisms or an increase in bacterial virulence. It has been estimated that 150 million episodes of UTI occur annually with $6 billion expenditure (1993).

UTIs can affect any age group or sex and are very common with the highest incidence in over 65 (40 % in females, 35 % in men). Accurate history, examination, and investigation are vital to determine if there may be an underlying cause of the urinary tract infection. Nearly 30 % of women have had a symptomatic UTI requiring antimicrobial therapy by age 24, and almost half of all women will experience a UTI during their lifetime. There is a 14 % chance of men having a UTI in their lifetime.

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The vast majority of urinary tract infections will have no underlying abnormality and will be effectively managed in the community with reassurance. Where the presentation is recurrent, investigation may be warranted especially in the older population.

Certain bacteria such as *Proteus mirabilis* and *Morganella morganii* may indicate underlying urinary tract calculi. The urinary tract becomes rapidly colonized once long-term stents or catheter is present. Bacteria will always be present on microscopy and culture in these instances. Antibiotic treatment is only required if the patient becomes systemically unwell or develops symptoms of foul smelling or cloudy urine.

Asymptomatic bacteriuria is also a common clinical finding especially in the elderly. Apart from excluding underlying disease, this finding only requires treatment in certain patient groups such as pregnancy and in children.

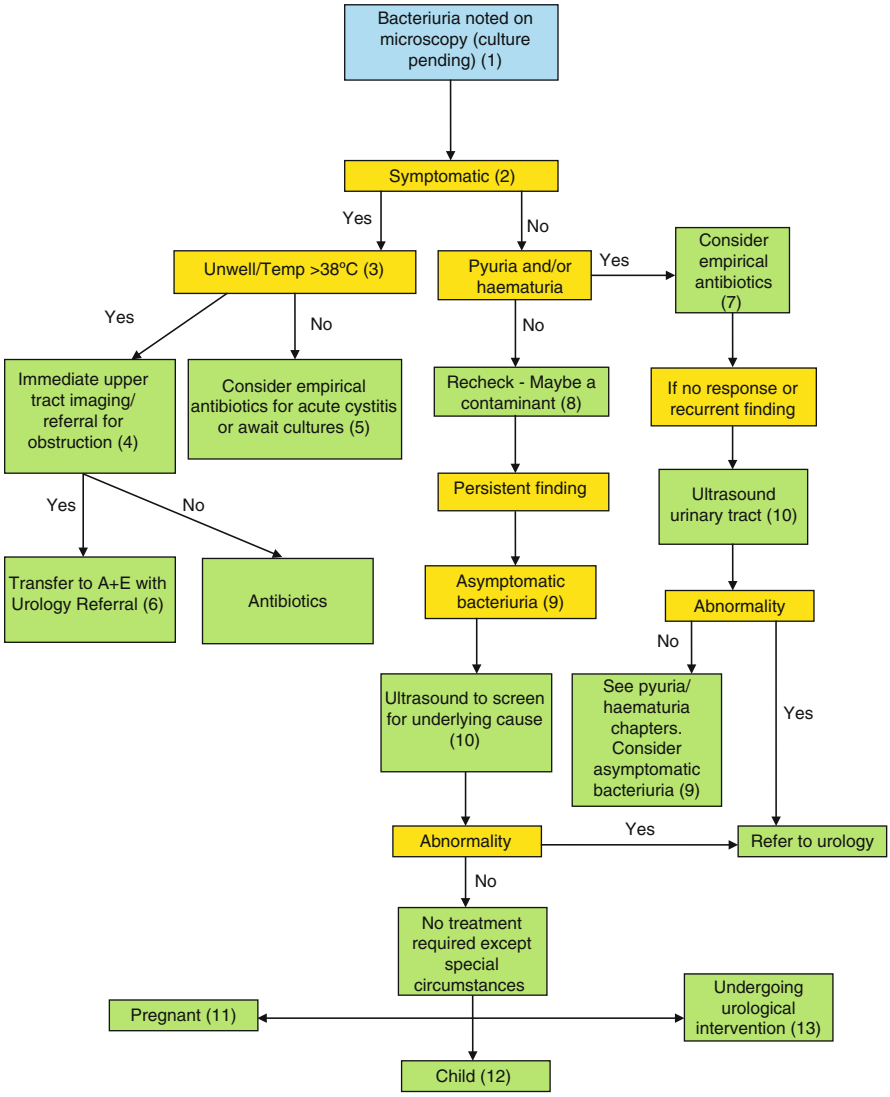
We hope this chapter provides a practical algorithm in how to manage the finding of bacteriuria on microscopy or culture and some of the common differential diagnoses.

Basic Investigation and Differential Diagnoses in Patients with Bacteria in the Urine

Comments About Flowchart 29.1

1. Urine should be collected in a sterile container and if not sent off immediately, can be refrigerated for 24 h. Patients with urinary symptoms should have urinalysis for bacteriuria, pyuria, and hematuria. This can provide evidence for a diagnosis of UTI to be made. The samples are usually now analyzed by automated microscopy analysis looking for bacteria. Bacteriuria is found in 90 % of infections with 10^5 CFU. However, it is often not detected with lower counts (10^2–10^4) and thus can give a false negative result. False positives with bacteriuria can occur with vaginal flora. Thus correlation with symptoms and other dipstick findings is important. The presence of bacteriuria has a sensitivity of 40–70 % and specificity of 85–95 %.

 If infection is suspected (bacteria, pyuria, or hematuria), the urine is then diluted and spread on culture medium. Each bacterium forms a colony on the culture plate and this is counted and adjusted per milliliter of urine (CFU/ml). Originally 10^5 CFU/ml was used as the threshold for clinical infection. This has been revised as clinically significant UTI in women can occur with 10^3 CFU/ml.
2. History and examination is crucial to the diagnosis and to whether intervention may be necessary. A clinical impression can often be gathered whether there is upper urinary tract or lower tract infection. Lower urinary tract symptoms of frequency, urgency, and dysuria may often be present. Urine dipstick may give early indication of infection by detecting white cells and nitrites. Nitrite testing is highly specific for infection.



Flowchart 29.1 Bacteriuria noted on microscopy

3. Where patients are clinically unwell, urgent referral and investigation may be warranted especially if there is a query of an infected obstructed urinary tract, e.g., urinary tract calculi or acute urinary retention. An urgent ultrasound examination can help the admitting physician narrow the differential diagnosis.
4. There can sometimes be difficulty in differentiating pyelonephritis from an infected obstructed system. Imaging can help reach the diagnosis; ultrasound may often show hydronephrosis. Secondary care services will be able to perform an intravenous pyelogram (IVP) or non-contrast computer tomography (CT) of

the urinary tract as required. These tests have a high sensitivity for detecting obstruction with identification of the underlying cause.

Ultrasound will also document the residual bladder volumes. Values consistently greater than 100 ml may give rise to persistent infection. Causes of high residual volumes include diabetes, cystocele, neurological disease, bladder outflow obstruction, detrusor failure, and voiding dysfunction. Patients should be referred to urology outpatients for further investigation and may need to be taught clean intermittent self-catheterization.

5. Acute cystitis refers to a principle infection of the bladder. This is more common in women and usually arises from ascending infection from vaginal or fecal flora. Lower urinary tract symptoms are common but systemic upset is rare. Recent sexual activity may often be noted. *E. coli* is the most prevalent organism and urine culture may only be required to confirm the diagnosis. Treatment with a short course (3 days) of empirical antibiotics such as trimethoprim, cephalexin, nitrofurantoin, or amoxicillin is usually sufficient for treatment. Bacterial culture may help guide treatment in resistant cases and should be checked when results are available.

 The following factors suggest a complicated urinary tract infection. Early referral should be considered if the patient presents unwell with the following:

 - Functional or anatomic abnormality of urinary tract
 - Male gender
 - Pregnancy
 - Childhood UTI
 - Elderly patient
 - Diabetes
 - Immunosuppression
 - Urinary tract instrumentation
 - Hospital-acquired infection
 - Symptoms for more than 7 days at presentation
 - Recent antimicrobial agent use

6. Patients can often become extremely unwell rapidly if gram-negative sepsis is not recognized on the background of acute colic. Early referral to A&E is recommended if there is no access to imaging facilities.

 The principles of management of an obstructed infected system are cultures, IV fluids, broad-spectrum antibiotics, and decompression of the urinary tract. Circulatory and renal support may sometimes be required in conjunction with the intensive care physicians. Decompression can be achieved by retrograde stenting in theater or placement of nephrostomy tube.

7. The finding of pyuria and hematuria is a good indicator of inflammatory response. The converse is also true – the absence of both suggests contamination or asymptomatic bacteriuria. Pyuria has a reported sensitivity of 80–95 % for UTI with a specificity of 50–76 %. Microscopic hematuria is found in 40–60 % of cystitis but absence does not exclude infection.

 The finding of recurrent pyuria can signify many abnormalities in the urinary tract and requires further investigation.

8. Contamination is common in patient-collected urine samples. Absence of pyuria suggests this and the sample should be repeated with advice given on how to collect the sample.
9. Asymptomatic bacteriuria can be present in a number of cases and needs treatment *only* in specific patient groups. The frequency of asymptomatic bacteriuria is:

 - Preschool girls – <2 %
 - Pregnant women – 2–9.5 %
 - Women aged 65–80 – 18–43 %
 - Men aged 65–80 – 1.5–15.3 %
 - Women aged >80 – 18–42 %
 - Men aged >80 – 5.4–21 %
 - Patients with indwelling catheters – up to 100 % (long term)

 Note: Pyuria can occur in asymptomatic bacteriuria. In this population, the presence of pyuria varies from 30 % in young females to 100 % in catheterized patients.

 One should bear in mind that urolithiasis may present in this way. Certain bacteria, such as Proteus, may raise suspicions of calculi. Chronic asymptomatic infection can give rise to staghorn calculi and in the long term give rise to destruction of the renal parenchyma. Renal calculi can be detected with >90 % accuracy using ultrasound although if suspected, the patient should also have a KUB x-ray.

 Screening and treatment of asymptomatic bacteriuria is recommended in pregnancy and before urological intervention. However, they are *not* recommended in any of the following situations:

 - Nonpregnant women
 - Diabetes
 - Healthy men
 - Patients with indwelling catheters, nephrostomy, or ureteric stents
 - Patients with spinal cord injury
 - Patients with candiduria
 - Patients in nursing homes/institutionalized
 - Immunocompromised or transplant patients

 There is no association between asymptomatic bacteriuria and uncomplicated UTI's/worsening renal function in these patients.
10. Ultrasound is a cheap, noninvasive test that will reliably demonstrate any abnormality in the urinary tract. The kidney should be checked for presence of hydronephrosis or stones. Scanning should be done with a full bladder to enable adequate examination and then a post void residual checked.

 In the absence of any other dipstick findings (no pyuria or hematuria), the necessity for upper tract imaging could be questioned. However, the finding of a Proteus or Pseudomonas species should prompt investigation to exclude stone. Routine cystoscopy in the absence of hematuria is not recommended if ultrasound examination is normal. If abnormalities are detected on US, referral to local urological services should be considered.

11. Asymptomatic bacteriuria occurs in 2–7 % pregnancies. Pregnant women *should be screened* for bacteriuria during the first trimester due to the 20–40 % risk of subsequent pyelonephritis. Bacteriuria is considered significant in asymptomatic women if two consecutive MSU samples grow the same organism with $>10^5$ CFU/ml. Women with positive cultures should have antimicrobial therapy for 3 days and follow-up cultures to confirm eradication. If bacteriuria is recurrent after appropriate treatment, then prophylaxis may be indicated.
12. Management of bacteriuria and UTI's in children is beyond the remit of this chapter. Asymptomatic bacteriuria can occur in 1–2 % of 5-year-old girls. Often it may be difficult to judge symptoms in children. It is thought that asymptomatic bacteriuria is a benign condition although there is no consensus on this. The EAU guidelines state that screening for bacteriuria is unlikely to prevent scar formation (which usually occurs early in infancy) and thus does not require investigation.

 NICE guidelines on proven urinary tract infection in children suggest that in infants less than 6 months, ultrasound imaging of the urinary tract should be sought within 6 weeks if there is an uncomplicated UTI. If this is a recurrent UTI, ultrasound should be obtained more urgently. After 6 months of age, a single episode of UTI does not need imaging; however, if this is recurrent or associated with atypical features such as raised creatinine, failure to respond to treatment within 48 h, or involve non-*E. coli* organisms, imaging should be requested alongside treatment.

 If there is an atypical or recurrent infection in a child less than 6 months, an ultrasound may be combined with a nuclear medicine renogram (DMSA) and micturating cystourethrogram looking for renal scarring and reflux, respectively. As the child becomes older, it is less likely to need such intensive investigation. In the very young, a low threshold for referral should be set for recurrent bacteriuria.
13. Patients who are to undergo urological intervention should be screened for infection and bacteriuria with preoperative midstream specimen of urine analysis (MSU). Treatment reduces the risk of postoperative sepsis and is thus recommended even in the asymptomatic.

 If there has been recent manipulation of the urinary tract, patients presenting with a sudden increase in lower urinary tract symptoms may have underlying infection. *Note*: MSU culture will always be positive in patients with indwelling catheters, stents, or if performing clean intermittent catheterization, as there is colonization of the urinary tract. These patients do not need treatment unless they become symptomatic, unwell, or note foul offensive urine.

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Chapter 30
How to Interpret the Results of a Midstream Specimen of Urine Culture Test

Philip Dundee and Matthew Frank Bultitude

Abstract Culture is performed in patients presenting with symptoms of urinary tract infection in order to confirm diagnosis, identify the infecting organism(s), and determine antibiotic sensitivities.

There are two ways in which urine is cultured: split agar, which is the most commonly employed method, and dipslide, which is a cheaper and simpler alternative to agar plating but has reduced sensitivity. It is dipped in urine, with the excess urine allowed to drain off before being placed in its plastic container, and is a test that can be performed at home.

Interpretation of culture requires an understanding of the common uropathogens, of proper collection technique, and of causes of both false-positive and false-negative results.

This chapter aims to provide an outline for the management of patients based on culture results.

Keywords Antibiotics • Asymptomatic • Bacteriuria • Culture • Cystitis • MSU • Pyelonephritis • Urinary tract infection • Uropathogen • UTI

Introduction

Midstream Specimen of Urine (MSU) culture is performed in patients presenting with symptoms of urinary tract infection in order to confirm diagnosis, identify the infecting organism(s), and determine antibiotic sensitivities. While some practitioners may omit urine culture in female patients presenting with an initial episode of

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uncomplicated acute cystitis, culture can still provide important information regarding antibiotic sensitivities, particularly in patients not responding to empirical antibiotics or those who then represent with recurrent infections. If culture is to be omitted, it is imperative that local bacterial resistance patterns are known. In all other female patients, and in all male patients, a urine culture is mandatory as part of the clinical work-up when urinary tract infection (UTI) is suspected.

This chapter aims to provide an outline for the management of patients based on culture results.

How to Interpret a Urine Culture

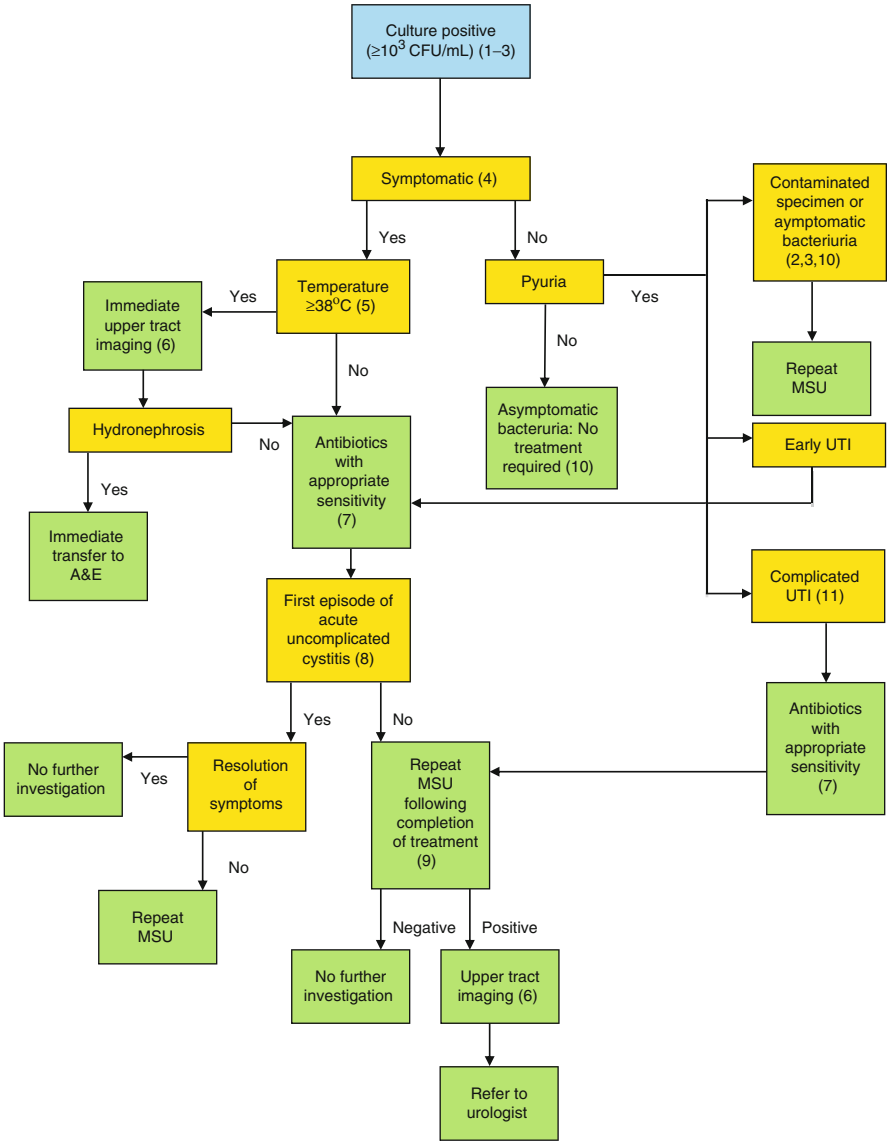
Comments About Flowcharts 30.1 and 30.2

1. There are two ways in which urine is cultured. The most commonly used is a split agar composed of one-half blood agar, which grows both gram-positive and gram-negative bacteria, and one-half desoxycholate or eosin methylene blue (EMB), which grows only gram-negative bacteria. Approximately 0.1 mL of urine is delivered to each half of the agar with a pipette and the plate is then left to incubate overnight. The number of colonies is then counted and multiplied by 10 to calculate the number of colony-forming units (CFU) per mL. The second technique is called a dipslide and is a cheaper and simpler alternative to agar plating but has reduced sensitivity. It is dipped in urine, with the excess urine allowed to drain off before being placed in its plastic container. One side of the slide is coated with a soy agar, a general nutrient for the growth of all bacteria. The second side is coated with either EMB or MacConkey agar for the growth of gram-negative bacteria. It is left to incubate overnight and the colonies counted. This can be done either visually or more commonly with an automated device. Only 1/100 to 1/200 mL of urine will attach to each side of the slide, so the count is multiplied by 100 or 200 to calculate the number of CFU/mL. Dipslides are generally sufficient for accurate diagnosis of urinary tract infections and are useful in patients suffering recurrent UTI, who are able to perform a culture with this technique at home.
2. The urinary tract, apart from the urethra, is usually sterile. Infections occur most commonly from ascent of perineal bacteria via the urethra and the most common uropathogens include *E. coli*, Proteus, *Enterococcus*, *Klebsiella*, and *Staphylococcus saprophyticus*.

 In a female patient presenting with clinical symptoms of acute, uncomplicated cystitis, $\geq 10^3$ CFU/mL of a known uropathogen is considered significant when obtained from a midstream urine specimen. Colony counts are not universal in all patients, however.

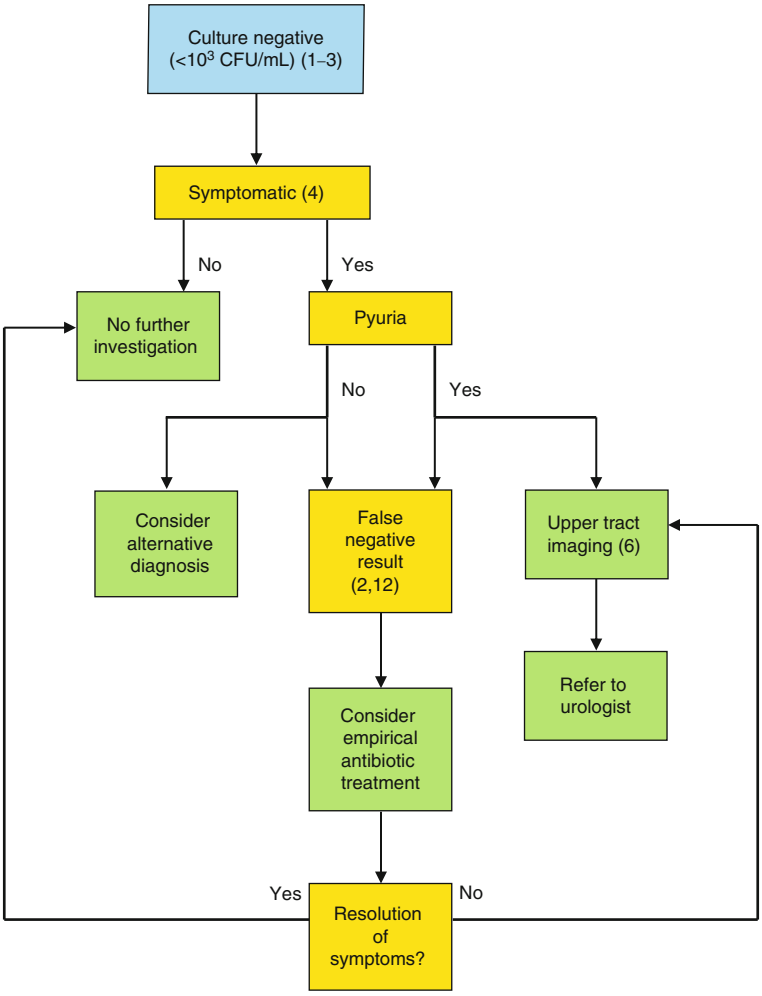
 In female patients with acute, uncomplicated pyelonephritis, $\geq 10^4$ CFU/mL is considered significant.

 In patients with complicated UTI, $\geq 10^4$ CFU/mL is considered significant in men (and from straight catheter specimens in women) and $\geq 10^5$ CFU/mL is considered significant in women. Any bacteria in a suprapubic aspirate are significant.



Flowchart 30.1 Positive culture

Proper collection technique is important to minimize the risk of both false-positive and false-negative cultures. In females, the labia should be parted and the introitus cleansed with moist wipes. The specimen is collected in a sterile container and refrigerated or processed immediately. False-negatives can occur with the use of antibacterial wipes, which may contaminate the voided specimen. In male patients, the prepuce must be retracted in uncircumcised men and the



Flowchart 30.2 Negative culture

glans cleansed with soap and water. The first 10 mL is usually discarded (hence the term MSU) as it represents urethral flora but may be processed separately if urethritis or prostatitis is suspected. In both men and women, false-positives may occur when the specimen is contaminated with perineal flora or if the specimen is allowed to stand at room temperature for prolonged periods. Perineal contamination should be suspected when there are high numbers of epithelial cells or when cultured organisms are not usually pathogens. If female patients are unable to separate the labia to obtain a specimen, a catheter specimen may be required.

3. Bacteria in any urine sample will rapidly multiply to $\geq 10^5$ CFU/mL in a number of hours. MSU samples must therefore be refrigerated or processed immediately to reduce the likelihood of a false-positive result.

4. Symptoms of urinary tract infection can range from mild frequency, urgency, and dysuria in cystitis to severe sepsis with circulatory collapse and shock. Loin pain with fever is suggestive of acute pyelonephritis, whereas perineal pain and urinary symptoms with or without fever may indicate acute prostatitis in men.
5. In patients with fever and positive urine culture, consideration should be given to hospitalization for IV antibiotics. In the absence of nauseas or vomiting, some patients may be managed in the outpatient setting with oral antibiotics. Ciprofloxacin is indicated as first-line treatment in febrile patients in the outpatient setting, except in cases of bacterial resistance or patient allergy. The clinician should always be alert to urinary sepsis in the setting of upper tract obstruction, a time-critical urologic emergency, which can rapidly progress to septic shock and death, even in young and fit patients. Upper tract imaging is therefore mandatory in all patients with fever and positive culture.
6. Upper tract imaging should include an initial renal tract ultrasound scan (USS). X-ray (XR) of the kidneys, ureters, and bladder (KUB) or computed tomography (CT) KUB should be considered if renal tract calculi are suspected. XR intravenous urogram (IVU) or CT IVU gives additional information regarding the anatomy of the upper tracts and some functional information regarding drainage of the upper tracts. CT is useful in providing information regarding differential diagnoses.
7. Culture reports will include identification of all significant cultured organisms. Mixed growth should be considered as contamination. Antibiotic sensitivities of all cultured organisms should be included in reports and are important for appropriate antibiotic selection in individual patients as well as providing essential epidemiological data. It is important to be aware of local bacterial resistance patterns such that appropriate antibiotics can be selected empirically, before culture results are available. Once culture results are available, antibiotics may be tailored to those with a narrow spectrum of activity. This will minimize the risk of side effects such as candidiasis and gastrointestinal upset.
8. An initial episode of culture or dipstick positive uncomplicated cystitis within 6 months should be considered as a first case. Recurrent UTI is defined as two or more episodes within 6 months or three or more episodes within 1 year. Recurrent UTI, complicated UTI, and a second UTI in a male patient under 35 years of age should be investigated with renal tract USS and/or IVU or CT IVU.
9. In female patients with recurrent acute uncomplicated cystitis, repeat culture is not always indicated if there is resolution of symptoms following antibiotic treatment. Repeat UTI after completion of therapy is, however, indicated if these patients are to be commenced on prophylactic antibiotics. In addition, patients with complicated UTI, pregnant women, and male patients with recurrent or febrile UTI should have repeat culture performed to ensure eradication of uropathogens.
10. Asymptomatic bacteriuria is the presence of $\geq 10^5$ CFU/mL in females or $\geq 10^3$ CFU/mL in males in the absence of symptoms. It does not require treatment except in pregnant women, children, and patients undergoing instrumentation of the urinary tract. Patients with bacteriuria and pyuria who are asymptomatic and have normal upper tract imaging do not require antibiotic treatment.

11. Any patient with a structural or functional abnormality of the urinary tract, or underlying host disease that interferes with normal immunological mechanisms, in the absence of symptoms but in the presence of positive cultures and significant pyuria should be treated with appropriate antibiotics. Notably, new onset offensive smelling urine in the absence of any other urinary symptoms, in the setting of positive urine cultures and pyuria, should *not* be considered asymptomatic. Alternatively, positive cultures, with or without pyuria, in asymptomatic patients should not be considered to represent UTI unless there is a complicating factor.
12. In patients with severe symptoms of cystitis, including frequency, urgency, and dysuria, voiding may be so frequent that colony counts more than threshold values for UTI are not reached, as the bacteria are not able to incubate and multiply within the urine for sufficient time to reach significant counts. If UTI is strongly suspected in these patients, they should be commenced on empirical antibiotic therapy.

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